Data Quality Management Policy

Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)

Version #	Effective Date
1.0	01JUL2025

Table of Contents

I. Overview 3
II. Significance of Data Entry Compliance 3
III. Data Quality Assessment Procedures 3
Review of Informed Consent Forms 3
Data Compliance Categorizations 4
IV. Corrective Action Measures for Non-Compliance 5
Site Check-In Calls 5
Corrective and Preventative Action Plan (CAPA) 5
Final Escalation Notification 6
V. Additional Considerations 6
Research Agreement Requirements 6
Coverage with Evidence Development (CED) Requirements 6
Compliance Thresholds Adjustments 6
Appendix A: 8
Appendix B: 9

I. Overview

The Data Quality Management Policy (DQMP) for the Alzheimer's Network for Treatment and Diagnostics (ALZ-NET) is intended to oversee all aspects of data quality and evaluation. Continuous data assessment will take place within a matrix that includes collaboration and communication between participating dementia practice sites and the ALZ-NET Data Management and Operations Teams.

A DQMP is essential for the success of ALZ-NET to:

- Adhere to the highest standards for data sharing and documentation.
- Ensure data integrity.
- Verify proper consenting practices at a site.
- Support the reliability of findings.
- Facilitate on-going data analyses.
- Provide clear corrective action parameters for data non-compliance.
- Contribute to improved clinical understanding and decision making that may impact patient outcomes.

This policy complies with the sponsor's obligations under CFR 312.50-56 and the data reviewer's obligations as detailed in ICH/GCP E6 5.18 (E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1).

II. Significance of Data Entry Compliance

Site adherence to the DQMP data entry guidelines is vital to upholding ALZ-NET's scientific integrity and enabling meaningful analysis of real-world care. Accurate and timely data entry further contributes to the overall success of the program and supports its core objectives.

Failure to enter required data in a complete, accurate, and/or timely manner may:

- Diminish the integrity of local and national data sets used to inform clinical decision-making guidance for physicians treating Alzheimer's patients.
- Compromise the regulatory-grade data needed to fulfill post-marketing requirements.
- Jeopardize patient access by prompting payer challenges, affecting reimbursement, and creating compliance risks tied to the registry's role in securing coverage.
- Require a site compliance audit or corrective action plan.

III. Data Quality Assessment Procedures

Review of Informed Consent Forms

An Informed Consent Form (ICF) review will be completed by ALZ-NET Operations Team remotely after a site's 10th patient is enrolled, and after every 50 patient enrollments thereafter (i.e. 50, 100, 150, etc.) in accordance with the following procedure:

- Email communication sent to site by ALZ-NET Operations Team with a random selection of four patient case ID numbers, along with the invitation to a site-specific Box folder managed by ACR.
- Site uploads ICFs within 30 business days.
- ALZ-NET Operations Team reviews the ICFs for completeness and accuracy of the following elements:
    - Verification that correct, IRB-stamped ICF version was signed.
    - Patient's printed name, signature, and date.
    - Patient's initials on optional component(s).
    - Person conducting consent discussion's printed name, signature, and date.
    - If applicable, LAR's printed name, signature, and date.
    - If applicable, LAR's initials on optional component(s).
- ALZ-NET Operations Team emails site with a summary report of the findings and instructions to address any errors.
- Site responds to queries within 90 days of receipt of the report and re-uploads the corrected ICFs into the Box folder for review, as applicable.

While it is strongly recommended that sites use Box for uploading patient ICFs, sites that are unable to do so may, as a last resort, utilize an alternative secure method approved by their institution. Any such method must ensure compliance with institutional and data security requirements and be coordinated with the ALZ-NET Operations Team.

Data Compliance Categorizations

The ALZ-NET Data Management team will evaluate site protocol compliance quarterly (four times annually), taking into consideration data completeness and timeliness. The quarterly compliance reports will coincide with the most recent ALZ-NET (A4709) Monthly Report that is sent to sites during the corresponding quarter. The compliance category assigned to a site will be reflective of their cumulative missing data and open queries. For additional categorization details, see Appendix A.

Sites will be categorized using a three-color grading scale as follows:

- **Green (Compliant)**: The site is consistently meeting ALZ-NET data submission requirements, with data being completed and on time in accordance with the corresponding thresholds for data compliance.
- **Yellow (Warning)**: The site is inconsistently meeting ALZ-NET data submission requirements, with data metrics falling into the corresponding threshold ranges. Site data is incomplete and/or past due.
- **Red (Non-Compliant)**: The site is significantly behind in data entry or has not responded to corrective actions, with data falling above the corresponding thresholds for compliance. If a site receives two consecutive, quarterly reports indicating a compliance status of 'Yellow (Warning), the site will also be designated as non-compliant.

IV. Corrective Action Measures for Non-Compliance

Site Check-In Calls

All sites that fall into non-compliant status will be required to attend a site check-in call with the ALZ-NET Operations Team before the next quarterly report date (90 days). The check-in calls will:

- Provide an opportunity for additional training to sites
- Covering the importance of query resolution and data completeness
- Allowing sites to ask questions.

Additional check in calls may be required for sites that fall into non-compliant status repeatedly through their duration of participating in ALZ-NET. Sites that fall into the non-compliant status repeatedly may be subject to further escalation measures, as determined by study leadership.

Corrective and Preventative Action Plan (CAPA)

A corrective and preventative action plan (CAPA) is a site-driven quality system plan that:

1. Identifies the area(s) of non-compliance.
2. Outlines the site's strategy to mitigate and prevent additional occurrences of non-compliance.

Non-Compliant Status: Sites that fall into non-compliant status for two consecutive, quarterly reporting cycles (6 months total) based on the threshold percentages listed in Appendix A will be required to submit a CAPA. Sites will have two weeks from the date a CAPA is issued via DocuSign (Appendix B) to complete and return to the ALZ-NET Operation Team. If queries and incomplete data are still not addressed by a site by the time the next quarterly evaluation report is issued, further escalation measures may be implemented, per the discretion of study leadership.

ICF Review Queries: Additionally, sites who do not resolve outstanding ICF queries within 90 days after receiving a summary report will also be required to submit a CAPA within 2 weeks from the date a CAPA is issued via DocuSign (Appendix B). An extension of an additional 90 days may be considered if a site communicates that more time is needed to resolve ICF queries due to needing the patient(s) to come on-site to the dementia practice to make the necessary ICF corrections.

Site responsibilities for completing the CAPA form include:

- Describing the nature of the non-compliance.
- Outlining steps and procedures taken to review and resolve the non-compliance.
- Describing any training implemented by site to address data non-compliance.
- Providing a time frame for when corrective actions will begin and resolution date of non-compliance.
- Principal Investigator (PI) attestation/signature acknowledging that corrective actions and procedures will be implemented by site.

Final Escalation Notification

Sites that fail to demonstrate CAPA progress in resolving outstanding data issues by the next quarterly report date (i.e. after three consecutive, quarterly reporting cycles of non-compliant status) or repeatedly fall into the non-compliant status intermittently may be subject to final escalation notification which will include the following measures:

1. Site will be evaluated for potential enrollment suspension until all data non-compliance issues are addressed/completed.
2. ALZ-NET study leadership will discuss possible termination of the site's participation from ALZ-NET.
3. Involve regulatory bodies such as the IRB, as applicable, if site termination is deemed appropriate.

V. Additional Considerations

Research Agreement Requirements

In accordance with the Research Agreement executed between the site and ACR, "The site will meet all guidelines and requirements as defined in the Protocol, or as provided by ACR in any instructions, manuals, policies, and correspondence, including any enrollment caps or timeframes specified in such guidelines and requirements."

Sites agree that ACR (or its representatives/agents) may review site data at agreed upon times during normal business hours. ACR will have access to the site's medical and research records and personnel to assess the research activities and ensure compliance with FDA regulations. ACR can also access the Principal Investigator and other personnel, research records, and relevant forms, either directly or remotely via secure methods, in accordance with applicable laws and the site's confidentiality policies. ACR will notify the site in advance and aim to minimize the length of the remote data quality assessment visits.

Coverage with Evidence Development (CED) Requirements

A site's continued participation in ALZ-NET is contingent upon adherence to the requirements defined in the Research Agreement between the site and ACR and Centers for Medicare and Medicaid's (CMS) requirements for coverage of FDA-approved monoclonal antibodies directed against amyloid for the treatment through the Coverage with Evidence Development (CED) pathway.

To maintain compliance with the requirements for coverage under CED through CMS, all CMS-approved studies, including ALZ-NET, must ensure that all aspects of the study are conducted according to appropriate standards of scientific integrity as identified by the Agency for Healthcare Research and Quality. Data quality, inclusive of both the completeness and accuracy of data for the duration of a study, is mandated as part of complying with the CED requirements for ALZ-NET.

Compliance Thresholds Adjustments

ACR reserves the right to adjust the compliance thresholds at any time. Adjustments to the thresholds may be implemented based on site feedback and performance, as well as ACR's

discretion to ensure the DQMP aligns with the objectives and metrics set forth by study leadership. The policy may be updated with adjusted thresholds as needed, and changes will be disseminated to sites in a timely manner.

APPENDIX A:

Corrective Action Parameters for Data Non-Compliance Table:

Criteria	*Corrective Action Plan for Site*
Compliant	
≤20% of a site's total patients have overdue/incomplete data forms. **AND** ≤25% of a site's total patients have open queries.	○ No action needed. ○ PI and site staff will receive email notices: - Monthly, with Data Query Reports to track data query and submission progress. - Quarterly, with compliance categorization.
Warning	
21 – 49% of a site's total patients have overdue/incomplete data forms. **OR** 26 – 49% of a site's total patients have open queries.	○ Site must resolve outstanding data items before next quarterly compliance report is issued (90 days). ○ Failure to improve from Warning to Compliant for two consecutive quarterly reporting cycles will result in site escalation to Non-compliant status. ○ PI and site staff will receive email notices: - Monthly, with Data Query Reports to track data query and submission progress. - Quarterly, with compliance categorization.
Non-compliant	
≥50% of a site's total patients have incomplete data forms **AND** ≥50% of a site's total patients have open queries.	○ Site will be flagged for immediate site check-in call with ALZ-NET Data Management Team. ○ Site must resolve outstanding data items before next quarterly compliance report is issued (90 days). ○ Failure to resolve queries and/or missing data before the next quarterly report will require site submission of a CAPA (See Appendix B). ○ Failure to make progress on outstanding data for three consecutive reporting cycles may result in further escalation at study leadership's discretion. ○ PI and site staff will receive email notices: - Monthly, with Data Query Reports to track data query and submission progress. - Quarterly, with compliance categorization.
OR Two consecutive, quarterly reporting cycles with Warning status.	

APPENDIX B:

ALZ-NET CORRECTIVE AND PREVENTIVE ACTION (CAPA)

Instructions: Please document data non-compliance, inclusive of missing and/or incomplete data entry, unaddressed data queries, and site unresponsiveness to requests in the sections below.

Specific instructions (orange lettering) for each section are located within the template. Please see the instructions and provide the actions to be taken by your site to identify and prevent future instances of non-compliance. Please note that all sections must be completed before submitting the CAPA through DocuSign. The CAPA must:

- Address all non-compliances specified.
- Include a description of how non-compliances identified will be resolved.
- Include a plan to ensure identified non-compliances will not recur as ALZ-NET progresses
- Include the role of the site Principal Investigator (PI) in preventing future occurrences of non-compliance.
- Include a review of **all** cited instances of data non-compliance as identified by the ALZ-NET Operations Team.

Return form to the ALZ-NET Operations Team at alz-net@acr.org within 10 days of request to submit CAPA. Failure to submit within this timeframe may result in further corrective action measures for your site. Please refer to the Data Quality Monitoring Program for ALZ-NET for details**.**

Protocol: Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)
Institution:
Site PI:
Site Check-In/Training Date:
CAPA Date:
Non-compliance Description:

Analysis of Non-compliance: *Describe the nature of the cause of the non-compliance*

Timeframe for Resolution of Non-compliance: *Provide information on when corrective actions will begin and the expected date of resolution of non-compliance*
Resolution: *Describe detailed steps taken to review and resolve the non-compliance; include new processes and procedures put into place. Attach any written processes, flow sheets, work instructions or SOPs if available. Include the role of the site PI, as appropriate.*
Date of Next Planned Assessment: *Indicate next date non-compliance will be reviewed.*
Training: *Describe in detail any training to be implemented, if applicable. Description should include when the training occurred or will occur, who will be trained, what is being trained, who will train the trainees, etc.*
Continual Process Improvement: *Describe in detail the steps to be taken to ensure this non-compliance does not recur as the study progresses, including how ALZ-NET will be monitored internally for adherence to the protocol, site-specific procedures, and GCPs. Include the role of the site PI, as appropriate.*

PI Attestation:
As the Principal Investigator, I will ensure that all corrective actions developed in conjunction with the research staff are implemented and completed. All research members assisting in the conduct of ALZ-NET are fully aware of their obligations in complying with the protocol and regulatory requirements.

_____ _____
Signature of Principal Investigator Date