ALZ-NET Data Sharing Policy

INTRODUCTION:

Those who are interested in asking research questions that utilize the data collected as part of the Alzheimer's Network for Treatment and Diagnostics (ALZ-NET) are encouraged to do so as a collaborative effort within the ALZ-NET structure. This approach will engage the ALZ-NET team's expertise of its own data set and will provide the best opportunity for a successful analysis. Requests to collaborate with the ALZ-NET team should be conducted through the processes and procedures outlined within this policy.

ALZ-NET may not be able to support all requests or the scope of certain requests for a variety of reasons, and therefore, the following policy for transfer of data to investigators for independent analysis is also outlined within this policy.

Responsible sharing of health data with academic institutions, industry (for-profit) organizations and government agencies is key to healthcare innovation and can lead to improvements in patient care, public health, research, and translation of discoveries to the bedside. Despite these potential benefits, there are significant risks when sharing data without appropriate oversight including patient privacy, legal compliance, financial exposure, and institutional reputation. This policy outlines ALZ-NET's established data sharing processes and demonstrates the commitment to efficiently and securely advance Alzheimer's disease and related dementia (ADRD) research initiatives.

Data from ALZ-NET will be shared with researchers and clinicians pursuant to the 2023 Final NIH Policy for Data Management and Sharing. According to the National Institutes of Health (NIH) policy, sharing scientific data accelerates biomedical research discovery, in part, by enabling validation of research results, providing accessibility to high-value datasets, and promoting data reuse for future research studies. The NIH policy champions making research available to the public to achieve these goals. The NIH states that it "recognizes that its data sharing policy efforts must flexibly evolve to keep pace with scientific and technological opportunities and notes that researchers' ability to generate, store, share, and combine data has never been greater," likely including the growth of real-world data (RWD). The NIH policy notes that "[s]hared scientific data should be made accessible as soon as possible. To protect participants' rights and confidentiality, personal health information (PHI) will be limited to the minimum necessary for authorized oversight before the data are shared.

ALZ-NET Code of Conduct:
All ALZ-NET Data Users will be expected to adhere to the ALZ-NET Code of Conduct.

SCOPE:

This policy provides information and guidelines for individuals and/or organizations wishing to request access to clinical, imaging, or biospecimen data (henceforth collectively referred to as 'data') that is archived with ALZ-NET. ALZ-NET and its sponsor, the Alzheimer's Association, are committed to providing researchers and clinicians in the Alzheimer's and dementia ecosphere an opportunity to access data collected through the network for purposes consistent with the goals of ALZ-NET. The Alzheimer's Association has contracted with the American College of Radiology (ACR) to provide for the management and operations of ALZ-NET. ACR, as an independent contractor, provides, among other things, certain services related to the

performance, delivery, provision of access to, and use of services in furtherance of ALZ-NET and/or the Protocol. All data collected, stored and shared through ALZ-NET is managed by ACR.

Purposes for data access may include, but are not limited to, design and execution of research studies, technology or product development, and educational initiatives. In the case of independent researchers, clinicians or for-profit organizations, requests should be of a research or educational nature or for purposes of technology or product development. The following policy is drafted to provide reasonable access to data while allowing the ALZ-NET team and leadership to meet its obligation of ensuring the data will be used responsibly, and that providing access will not burden ALZ-NET resources such as to impede its ability to pursue its primary study (NCT#06170268) or affiliated study(ies) objectives.

Prior to submitting a grant proposal indicating that clinical, imaging, and/or biospecimen data archived by ALZ-NET will be used to conduct the proposed research, an investigator should submit a request and obtain written approval from ALZ-NET. ALZ-NET treats such requests as it does any other request, as detailed below.

POLICY:

Data Access and Use Committee (DAUC):
The ALZ-NET Data Access and Use Committee (DAUC), formerly known as the ALZ-NET Research and Publications Subcommittee, is charged with overseeing the transparent, consistent, and responsible sharing of ALZ-NET wide health data. The ALZ-NET DAUC will provide the necessary oversight and protections of the Data Access and Use Request (DAUR) applications and use of the ALZ-NET related data. Following best practices, the DAUC consists of a reasonable number of members - no more than 15, no less than 9 - covering multiple relevant areas of expertise. Appointed members represent senior management of ALZ-NET; experts in data management, ethics, relevant research areas and potentially a data sharing advocate; representatives from the site network; and up to three independent representatives outside of the ALZ-NET team to help address the issue of conflicts of interest and to prevent "data hoarding" by internal researchers. Essential to the goals of ALZ-NET, the DAUC also includes representatives from historically underrepresented community partners and health systems to ensure requests are in line with equitable standards and practices.

The DAUC will convene, at minimum, quarterly to review submitted DAURs through the ALZ-NET webform. Ad hoc committee meetings will convene as needed for other requests or high volumes of requests.

The DAUC is responsible for reviewing and determining the status of application requests for archived clinical, imaging, and/or biospecimen (when available) data. At minimum, 70% of the DAUC must approve a request to enable data and/or sample sharing.

DAUC Membership Includes:

- Chair, who has expertise on ALZ-NET data elements, components of the data collected and the formats collected
- ALZ-NET lead statistician
- At least two members of the ALZ-NET team, including expertise with health disparities and patient experience

- At least two representatives from participating ALZ-NET sites (these may also be study team investigators)
- Lead statistician at Brown University School of Public Health
- At least one senior researcher in Alzheimer's dementia, invited from the research community at large or study advisors
- ACR and Alzheimer's Association representatives (non-voting)

An updated list of committee members can be found on alz-net.org.

Submission of Data Access and Use Request (DAUR):
Before data are made available for use, a Data Access and Use Request (DAUR) must be submitted for review and approval by the ALZ-NET Data Access and Use Committee (DAUC). Detailed instructions concerning how to access ALZ-NET's archived clinical, imaging and biospecimen data are available on the ALZ-NET website. The DAUR form and applicable instructions are also located on the website. All DAURs must be electronically submitted.

Before submitting a DAUR, please ensure the following: (1) proposed analyses must be hypothesis driven; (2) attest to use planned analyses for research-grade, peer-reviewed publications; (3) there is no overlap to the existing ALZ-NET protocol CED aims, objectives and additional planned analyses to ensure there is no overlap prior to application submission; and (4) must provide a sample size estimate and define case inclusion criteria as part of the DAUR application.

All required fields within the DAUR must be completed in entirety. At minimum, requestors need to provide the following information:

- The project title
- Names and titles of key project personnel
- A non-confidential research statement with confirmation of adherence to all relevant laws, regulations, and institutional policies
- Project proposal (inclusive of brief description, hypotheses, strategic aims, and/or planned analyses)
- Date range of data
- Level of data access (safe harbored de-identified data set or limited data set)
- Type of data being requested (clinical, imaging (DICOM), and/or biospecimen (samples or data) when applicable
- Data elements being requested
- Information regarding funding sources, if applicable.
- Contact information for the requester, including name, email, and affiliation.

Once submitted, the ALZ-NET DAUR will be reviewed by the ALZ-NET DAUC. The DAUC will conduct their review and issue one of three responses to the requestor.

1) Approved
2) Rejected and invited to resubmit with more information
3) Rejected

Upon approval, the requester will be put in contact with staff from ACR to facilitate access to the data. DAUR approval will remain in effect from one year after approval is granted and will be valid for up to three years. A formal data use agreement (DUA) must be executed for the entire term of a DAUR, prior to access being granted. ALZ-NET represents RWD being collected

longitudinally; as a result, the DUA will be for a specific data duration which must be specified within the request. DAURs and DUAs can be renewed.

Those rejected and invited to resubmit or rejected will receive information about the reasoning for the decision.

Data Types and Formats Available:
ALZ-NET uses a set of protocols and procedures to collect, standardize and archive data and materials from participants. All data and materials available for sharing are de-identified into a limited data set (e.g. only including dates of service) and adhere to strict standards for protecting data and privacy. To ensure de-identification of brain imaging studies, skull stripping on any axial brain imaging will occur prior to sharing externally. Skull stripping will ensure that users will not be able to leverage facial recognition technology to re-identify patients. This process is in addition to standard metadata de-identification that is applied to all available DICOM files.

ALZ-NET's image repository provides requestors access to real-world, longitudinal brain imaging including MRI, amyloid PET, FDG PET, and tau PET. Deliverables associated with the image fee schedule may include the DICOM files, a study inventory, and supporting documentation describing modalities, sequences, metadata, and Limited Data Set (LDS) processing. ALZ NET maintains full transparency about data provenance, processing, and known limitations. Requestors are encouraged to contact the ALZ-NET Operations Team to ensure clear understanding of dataset characteristics and appropriate use.

Image Specifications and Processing:

DICOM studies are submitted to ALZ-NET by participating ALZ-NET sites and imaging facilities through ACR's secure TRIAD™ platform. Images are handled in accordance with the ACR's ALZ-NET imaging specifications and processes outlined in the ALZ-NET Imaging Specifications Quick Guide. Images are processed into a Limited Data Set (LDS) using ALZ NET de-identification rules that remove identifying metadata, clean description fields, retain scientifically meaningful dates, and apply pixel-level PHI redaction tools. Imaging is retained in its original form (after anonymization) to preserve real-world acquisition characteristics and is organized chronologically to support disease-progression and biomarker research.

Data collected by ALZ-NET include longitudinal clinical, imaging, and safety data and will be cached every six months for sharing. Participating ALZ-NET sites are required to adhere to the Data Quality Management Policy (DQMP), which outlines continuous data assessment and compliance responsibilities for participating ALZ-NET sites.

While ALZ-NET strives to maintain high data quality, users should be aware that datasets may contain open (unanswered) and/or unresolved (unreviewed) data queries at the time of access. Completeness may vary across participants and data types. Data users are expected to interpret findings with these considerations in mind.

ALZ-NET utilizes a comprehensive internal ALZ-NET specific Data Management Plan to ensure the highest level of data accuracy as is possible in a real-world data set. Data cleaning initiatives rely on a combination of automated and manual processes:

Automated

- Programmed edit checks fire queries as soon as the eCRF is saved (Site from System)
- Email notifications to the Data Management Team to prompt review of high priority items (e.g., patient death, adverse event, lost to follow-up, withdrawal of consent). Manual review performed in near real time.
- "Sticky Notes" functionality to alert the Data Management Team of the need to review forms related to patient status, death, and/or adverse event.

Manual

- Review of site query responses (minimally every 2 weeks) resulting in either closing the query or re-querying for additional information.
- Data listings run to review data points on a single eCRF across all patients
- BO4 reports created/run to review specific data points across multiple eCRFs across all patients.
- SAS reports created/run by programming to assist the Data Management Team in their review/reconciliation.
- Collaboration with the ALZ-NET Statistical Analysis Team and ongoing data cleaning surveillance.

Answered queries are reviewed and closed/re-issued on a continual basis by the system and ALZ-NET Data Management Team across all patient forms and by case. A detailed listing of pre-programmed automatically issued queries (i.e., edit checks) by variable name can be found here.

In addition to prioritizing oldest queries first, participating sites are instructed to prioritize answering queries and performing data entry associated with the following data forms and elements:

- Patient Participation Status:
  - Baseline and Follow-up status forms
  - Participation end point (patient death, withdrawal of consent, lost to follow up)
- Adverse/ARIA Event Reporting
- Novel Therapy forms (Admin YN, Novel Therapy-specific) at Baseline and Follow-up
- Diagnostic Testing log
- Additional Assessments:
  - MMSE/MoCA and FAQ (required)
  - NPI-Q and AD8 (optional)
- Clinical Features form
- Imaging Submission log and submitted radiology data
- Medical History updates
- Changes to Concomitant Medications

Users of these data are responsible for issuing appropriate data integrity disclosures in any works that result from analysis of the provided data sets, including, but not limited to:

- Extent of Missing Data: Identification of any missing fields in submitted forms, particularly those related to ARIA documentation, therapy exposure, and/or Adverse Event reporting.
- Open or Unresolved Queries: Summary of outstanding data queries that may affect interpretation, including unresolved discrepancies in scan timing, therapy status, or clinical assessments.

- Incomplete Form Submissions: Acknowledgment of any partially completed ALZ-NET forms or deviations from standardized reporting templates.
- Source Data Limitations: Disclosure of known limitations in source systems (i.e., EHRs) that may impact completeness or consistency of submitted data.

Any relevant data analysis disclosures will be provided to the requestor by ALZ-NET at time of data transfer.

A high level summary of data collected by ALZ-NET can be viewed via the Summary Table of Data Elements. Requestors should keep in mind that data cleaning is an ongoing process. Data available for sharing have been reviewed and cleaned, first via the use of logic and other checks during the process of web based data entry, second via review by Data Management Center staff, and third, via review by Biostatistics Center staff. The process of obtaining clarification of illogical and suspect data is ongoing. Query reports are available for approved requests.

Clinical data can be provided to approved requestors in the following formats: delimited files (CSV, comma, pipe, etc.), SAS datasets, or SAS transport file. Imaging data will be provided in DICOM format.

Sample Selection Process Summary:
Eligible cases are identified across all participating sites based on predefined inclusion criteria determined by the requestor. To ensure fairness and reduce systematic bias, both the order in which sites are considered and the selection of cases within each site are randomized. During each selection round, one eligible case is randomly chosen from each site, following a randomly generated site order. Rounds continue sequentially until the required sample size is reached or all eligible cases are exhausted. This process promotes balanced representation across sites while maintaining transparency, reproducibility and generalizability. Requestors may specify alternative or additional selection criteria, stratification needs, or prioritization rules, which will be applied prior to random selection and documented accordingly.

DAUR Review Considerations:
The DAUC will review each submitted DAUR with the following considerations:

- Scientific merit and validity of the proposal.
- Availability of the data requested. In some cases, data elements requested may not be available and/or may not have sufficient collection to share in aggregate to ensure the patient's privacy and protections. If this is the case, the committee may recommend a resubmission at a later date when the data might be available.
- Operational reasonableness of the request; in some cases, DAURs may include frequency and/or formatting of data sharing that are untenable.
- Consistency between the scope of the DAUR and the scope of the scientific project for which the data will be used.
- Qualifications of the requestor (i.e. does the requesting party have sufficient resources to carry out the project in the timeline proposed?)
- Significant overlap with existing studies, including ALZ-NET defined aims and ALZ-NET approved affiliated studies. More information about ALZ-NET approved affiliated studies

is here. The DAUR is specific to ALZ-NET and not for data generated through affiliated studies.

- Requestor country of origin. Pursuant to Executive Order 14117, requests for data from entities or individuals in Countries of Concern or from a Covered Person will not be considered.
- Application is for research and/or educational purposes with intent of publishing. In keeping with ALZ-NET's commitment to transparent, real-world evidence generation, each research proposal must include a clear intent to publish and publicly share research findings or educational findings.
- Requestor agreement to obtain Institutional Review Board (IRB) approval prior to data delivery.

The above considerations are subject to change and are widely promoted via the ALZ-NET website. The DAUC reserves the right to terminate data access at any time if it is determined that the data are being misused, ethical standards are not upheld, or there is a violation of the data use agreement (DUA, described below).

Execution of Data Use Agreement (DUA):
In order to access the data collected through ALZ-NET, an ALZ-NET specific data use agreement (DUA) must be executed between the American College of Radiology (ACR), on behalf of the Alzheimer's Association, and a research institution (or directly with the researcher in the case of a citizen scientist who is not affiliated with an institution). To submit a copy of the DUA, the template agreement can be downloaded from the ALZ-NET website. This agreement will outline the terms and conditions of data access, including data usage restrictions, data security, and privacy protections.

Note: DUAs can only be signed by Authorized Institutional Officials who have the authority to bind all users at their institution to the terms of the DUA. With the exception of citizen scientists not associated with institutions, individual researchers cannot sign their own DUAs with ACR.

DUAs will remain in effect for two years from the DUA Execution Date, unless otherwise negotiated. They will automatically expire at the end of this period unless terminated or renewed. ALZ-NET has a follow up process in place to monitor proper use of data, completion of the intended work, and extension of the DUA if applicable.

Requesters will also be responsible for any associated fees or costs, as specified in the agreement.

Sharing Requestor Application Details for Public Visibility:
To promote transparency and foster trust in ALZ-NET's research initiatives, ALZ-NET will publicly share high-level information about project requests on the ALZ-NET DAUC website, including the requestor's name, affiliated institution, project title, and a brief summary of the research purpose. This information is shared solely to provide visibility into the types of projects utilizing ALZ-NET data. A corresponding statement will be included in the DUA informing requestors that certain application details may be made publicly viewable.

Requirement for Institutional Review Board (IRB) Approval Prior to Data Release:
Requestors must provide evidence of IRB approval to receive, access, and use ALZ-NET data. Both the ALZ-NET authorization to release data and the requestor's authorization to receive and use the data must be satisfied before any transfer can occur under the DUA. Acceptable forms of documentation include IRB approval letters, IRB determination letters (e.g., Not Human Subjects Research, Exempt), and/or written confirmation from an authorized institutional oversight body (e.g., Research Compliance Office, Human Research Protection Program). Self-attestation or investigator-signed statements are not sufficient. For international requestors, approval may be obtained from an Ethics Committee, Research Governance Office or equivalent institutional or regulatory authority. Terminology may differ across countries, but the requirement for externally verified institutional approval remains the same.

Acknowledging ALZ-NET in Publications and Presentations:
Acceptance of ALZ-NET data obligates the recipient to acknowledge ALZ-NET in all publications and presentations, including the date of data access, and relevant ALZ-NET project details, in accordance with the ALZ-NET Data Use Policy, as below:

Acknowledgment Statement: The analyses described in this *[publication/report]* were conducted with ALZ-NET data (*[link]*). accessed on *[date]*. ALZ-NET is sponsored by the Alzheimer's Association, who has contracted with the American College of Radiology (ACR) to provide for the management and operations of ALZ-NET. ALZ-NET is advised by a group of leading clinicians and researchers, as well as partner organizations. This research was made possible because of the patients who provided their consent to share their information and the providers and organizations (www.alz-net.org) who contributed to the real world patient data of ALZ-NET..

Reporting Outcomes From ALZ-NET Use Back to ALZ-NET:
ALZ-NET Data Users are expected to adhere to the ALZ-NET Code of Conduct's requirements for reporting materials generated from ALZ-NET data, including, but not limited to, publications, presentations and recruitment materials.

It is expected that studies using ALZ-NET resources publish and share findings related to that analysis with the scientific community within 12 months of the analysis being carried out. Should publications result from the use of ALZ-NET resources now or in the future, the recipient agrees to notify the ALZ-NET DAUC with appropriate details (e.g. reference, PubMed and PubMedCentral ID#) and provide a copy of the publication and a summary of outcomes and findings within 30 days of publication so productivity derived from the ALZ-NET resources can be reported to the funding Sponsor, Alzheimer's Association, and linked through the ALZ-NET website. This should also include a lay language summary of the use and outcomes for sharing publicly.

Should new funding result from research using ALZ-NET data now or in the future, the recipient will be required to notify the ALZ-NET DAUC within 30 days of the award and provide appropriate details (e.g. grant title, sponsor, number, dollar total, dates) so productivity derived from ALZ-NET resources can be reported to the Alzheimer's Association. Failure to comply with the requirements outlined in the DAUC/DAUR may result in the requestor and their team being restricted from accessing ALZ-NET data in the future.

FEE STRUCTURE:

Clinical Data:

	ALZ-NET data contributing site[5]	Academic/non-profit organization - Non data contributing	Non-academic or for-profit entity
Data Transfer Specification (DTS) Development[1]	$1,000	$2,500	$7,500
Data QC and Transfer[2]	$750 per transfer	$1,000 per transfer	$3,000 per transfer
Data Source Fee[3]	No Fee	$50/site	$300/site
Infrastructure Fee[4]	No Fee	15% of data sub-total	45% of data sub-total

1) A document that defines method, format, and frequency for the electronic transfer of data for a specific project
2) Quality Control (QC) - Tasks associated with preparing data files for transfer and confirming accurate programming of the curated data set through a secondary review process to ensure fulfillment of the approved DAUR.
3) Supports the costs related to ALZ-NET's data acquisition, processing, compliance, and technical support of the external data sources (i.e., participating sites). Calculated based on the number of participating sites that contribute data towards the data set of the approved DAUR. Fee applies to each official data transfer.
4) Supports the costs of the underlying operational infrastructure of ALZ-NET. Rate is applied to the subtotal of the data related fees associated with the approved transfer.
5) A participating ALZ-NET site that has registered and provided clinical data for at least 10 patients and wants data beyond their site data.

Note: Federal entities, such as Centers for Medicare & Medicaid Services, who request the ALZ-NET data will have requests reviewed by the DAUC Committee and managed independently of this fee structure.

Imaging Data:
Associated fees for access to DICOM imaging data are dependent on the scope of the request. A final fee structure will be determined after review and approval of the DAUR. Variables in consideration will be the volume of images and any processing of the images beyond ALZ-NET's standard processing pipeline. ALZ-NET's standard imaging fee schedule entails:

	ALZ-NET data contributing site[5]	Academic/non-profit organization - Non data contributing	Non-academic or for-profit entity
Data Transfer Specification (DTS) Development[1]	$1,000	$2,500	$7,500
Imaging Data QC and Transfer[2]	$750 per transfer	$1,000 per transfer	$3,000 per transfer
Imaging Data Source Fee[3]	No Fee	$2 per imaging study	$7 per imaging study
Imaging Infrastructure Fee[4]	No Fee	15% of imaging data sub-total	45% of imaging data sub-total

1) A document that defines method, format, and frequency for the electronic transfer of data for a specific project. Fee associated with imaging data is waived if clinical data is also included in the approved request.
2) Quality Control (QC) - Tasks associated with preparing data files for transfer and confirming accurate programming of the curated data set through a secondary review process to ensure fulfillment of the approved DAUR.
3) Supports the costs related to ALZ-NET's data acquisition, processing, compliance, and technical support of the external data sources (i.e., participating sites). Calculated based on the number of imaging studies that contribute towards the data set of the approved DAUR. Fee applies to each official data transfer.
4) Supports the costs of the underlying operational infrastructure of ALZ-NET. Rate is applied to the subtotal of the data related fees associated with the approved transfer.
5) A participating ALZ-NET site that has registered and provided clinical and/or imaging data for at least 10 patients and wants data beyond their site data.

Note: Federal entities, such as Centers for Medicare & Medicaid Services, who request the ALZ-NET data will have requests reviewed by the DAUC Committee and managed independently of this fee structure.

Biospecimen Samples and/or Biospecimen Data:
Although not currently available, there will be a future opportunity to request biospecimens and/or associated data. Associated fees for access to banked biospecimen data will depend on the scope of the request. A fee structure will be determined after review and approval of the DAUR. Variables in consideration will be the number of samples being requested and any additional processing of the samples, and shipping costs. Upon completion of the analysis, researchers are required to return the raw data to the ALZ-NET Team prior to unblinding the samples.
When these biospecimen samples are available, these requests may also include data generated from sample analyses. These requests are subject to a different fee structure, as they do not involve shipping or material costs. Data sharing will be limited to instances when the ALZ-NET Team is able to perform the sample analyses.

Affiliated Studies:
DAUR through this process does not include requests related to affiliated studies. Associated fees and costs for affiliated studies are dependent on the scope of the project. Overall budgets will be determined in collaboration between the affiliated study and the ALZ-NET Leadership Team. For more information on affiliated studies, visit https://www.alz-net.org/affiliated-studies.

ENFORCEMENT:

This Policy was developed by the ALZ-NET Leadership team and has full support and approval from its ALZ-NET partners. Failure to comply with this document may result in a termination of data access request capabilities.

Contact Information: Please direct all policy questions or comments to the ALZ-NET Operations Team by emailing alz-net@acr.org.

REVIEW AND UPDATES:

This Policy will be reviewed periodically and updated as necessary to reflect changes in regulations, best practices, and the evolving needs of ALZ-NET. This policy is subject to change, and all data access requests will be governed by the version of the policy in effect at the time of the request.