

From Fit-for-Storage to Fit-for-Purpose: NCRAD's Approach to Biospecimen Quality in Alzheimer's Disease Research

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Background

- AD/ADRD research has expanded beyond genetic discovery to include transcriptomics, cell-based modeling, fluid biomarkers, and multi-omic analyses.
- As downstream applications have diversified, biospecimen quality must be defined by more than **collection and storage integrity**.
- A "high-quality" biospecimen is increasingly **application-dependent**, requiring documentation, traceability, and QC attributes aligned with the intended research use.
- NCRAD's experience supporting national, multi-site AD/ADRD studies provides a platform for operationalizing a **fit-for-purpose quality framework**.

Why Fit-for-Storage Is Not Enough

- Traditional biospecimen quality emphasizes whether specimens were **collected, processed, and stored correctly**. These criteria remain essential, but do not fully determine whether a specimen is **suitable for a specific downstream research application**.

Fit-for-Storage	Fit-for-Purpose
Collection completed correctly	→ Collection aligned with intended downstream use
Processing and storage standardized	→ Preanalytical variables documented and reviewed
Specimen stable and retrievable	→ Relevant QC attributes available for interpretation
Repository standards met	→ Specimen is research-ready for specific application

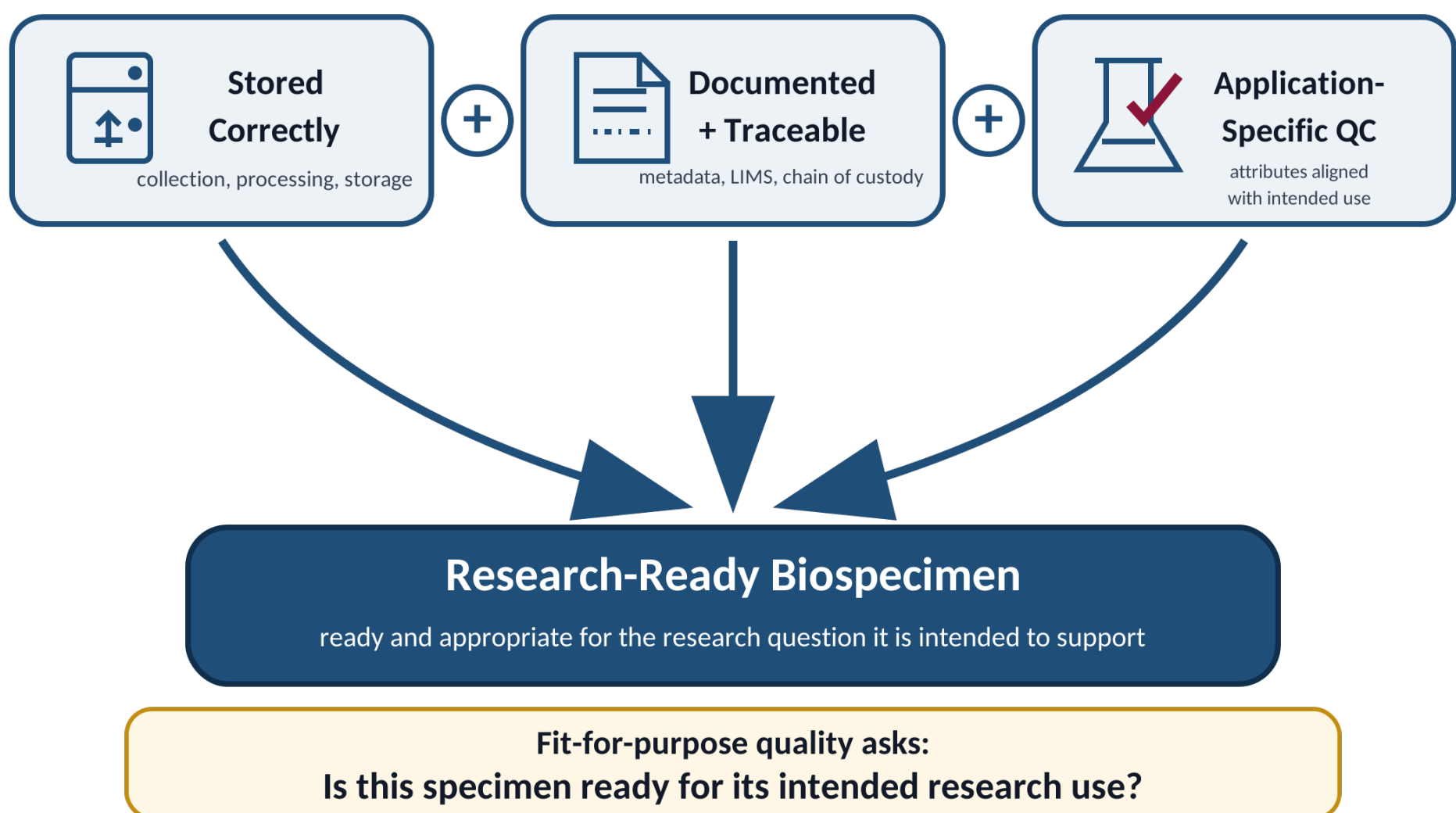
Core idea: A specimen can be stored correctly but still not be fit for a specific research purpose.

Objective

- To describe how NCRAD operationalizes a **fit-for-purpose biospecimen quality framework** across diverse AD/ADRD specimen types and downstream research applications.
- This framework emphasizes **research readiness, traceability, preanalytical documentation, and application-specific QC**.

Key Concept

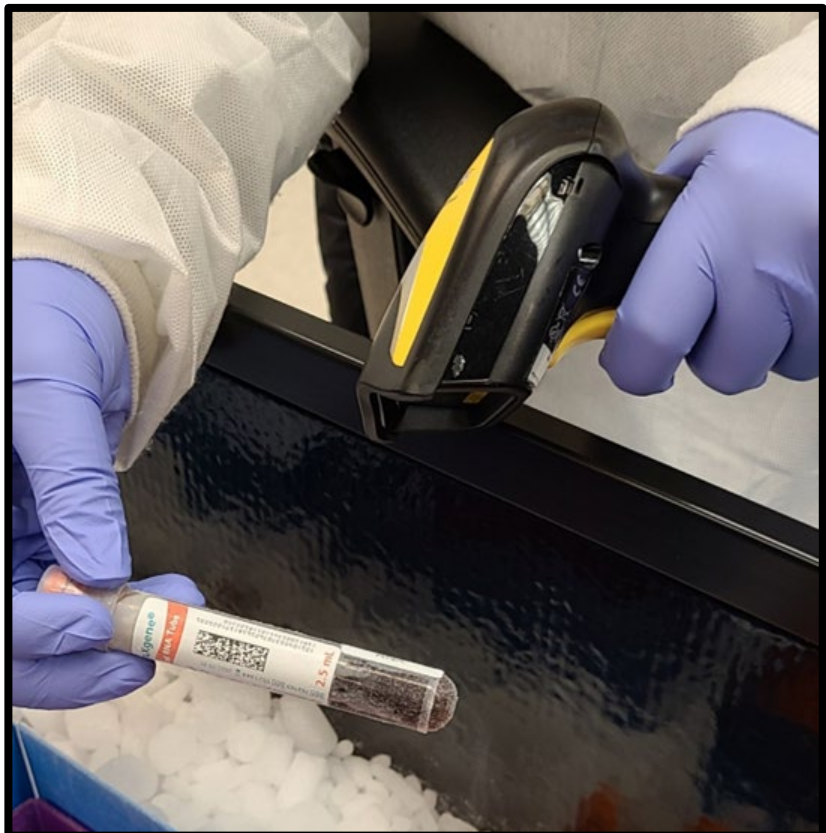
Biospecimen Quality Is Application-Dependent



NCRAD Fit-for-Purpose Quality Framework

- NCRAD applies a biospecimen quality framework as a **lifecycle process**, beginning before specimen collection and continuing through distribution and data return.
- Each step is designed to preserve specimen integrity, document preanalytical variables, and align QC with **intended downstream research use**.
- Quality is built into every step of the workflow rather than assessed at a single endpoint.*

Operationalizing Fit-for-Purpose Quality Across the Biospecimen Lifecycle



Fit-for-Purpose Quality Workflow

A lifecycle approach linking biospecimen handling to downstream research readiness

Quality is built across the specimen lifecycle

- Study Design & Research Intent**
Define anticipated specimen use and downstream applications
- MOP / Collection Kit Development**
Standardize materials, labels, handling, and site instructions
- Site Training & Specimen Collection**
Reduce preanalytical variability across multi-site studies
- Accessioning & Preanalytical Review**
Document receipt conditions, labeling, and collection variables
- Specimen-Specific Processing**
Align workflows with DNA, RNA, PBMCs, iPSCs, plasma/serum/CSF, stool, etc.
- QC & Identity Verification**
Assess attributes relevant to intended research use
- Storage, LIMS & Traceability**
Maintain lifecycle documentation and chain-of-custody oversight
- Distribution & Data Return**
Support responsible sharing, assay result return of data, and future discovery

Quality Lenses Applied Throughout

- Preanalytical Variables
- Identity
- Integrity
- Traceability
- Application Suitability
- Governance & Sharing

These dimensions inform decisions at each stage rather than at a single endpoint.

Outcome

Long-Term Scientific Value

Research-ready biospecimens matched to intended scientific use



Specimen-Specific QC Considerations

Fit-for-purpose quality requires measurable QC attributes and preanalytical variables interpreted in the context of downstream use.

Specimen	QC Measures / Variables	Downstream Use
DNA	SNP fingerprinting; Concentration; A260/280; A260/230; DIN or Fragment Size	Genotyping GWAS; WES/WGS Long-read sequencing
RNA	Concentration; A260/280; A260/230; RIN; DV200 when needed	RNA-seq Expression profiling miRNA analysis
PBMCs	Viable cell count; Post-thaw viability and recovery; Processing time; Cryopreservation conditions	Immune profiling Functional assays iPSC generation
iPSCs	Identity; Sterility; Mycoplasma; Passage Number; Viability; Morphology; Karyotype; Pluripotency / Differentiation QC	Disease modeling Functional genomics Therapeutic screening
Plasma / Serum	Hemolysis; Turbidity; Volume; Processing time; Centrifugation conditions; Storage temperature; Freeze-thaw history	Fluid biomarkers Proteomics Metabolomics
CSF	Hemoglobin contamination; Volume; Processing time; Centrifugation conditions; Storage temperature; Freeze-thaw history	Fluid biomarkers Proteomics Metabolomics
Stool	Collection preservative; Time to stabilization; Storage temperature; Freeze-thaw history	Microbiome Metagenomics Metabolomics
Brain Tissue	Brain region; Preservation method; Postmortem interval; H&E/pathology	Neuropathology Transcriptomics (spatial) Molecular profiling

Key point: QC measures are specimen-specific, but interpretation is application-dependent

Fit-for-Purpose Outcomes

A lifecycle quality framework enables biospecimens to be selected, interpreted, distributed, and shared with greater confidence.

- Application Aligned Workflows**
Collection, processing, and QC reflect specimen type and anticipated research use.
- Lifecycle Documentation**
Specimen history, preanalytical variables, storage, QC, and metadata are captured.
- Identity + Integrity Confidence**
Identity checks and quality measures reduce uncertainty before downstream use.
- Scalable Research Support**
Centralized workflows support evolving AD/ADRD applications across studies.
- Data Return + Governed Sharing**
Returned assay data and governed sharing extend long-term scientific value.

Outcome: fit-for-purpose quality increases confidence that each specimen is appropriate for its intended research use.

Conclusion

- Biospecimen quality is best defined by **fitness for intended research use**, not storage integrity alone.
- NCRAD's centralized infrastructure supports **research ready biospecimens** across diverse AD/ADRD specimen types and downstream applications.
- Specimen-specific QC, lifecycle documentation, governed specimen sharing, and data return support **long-term scientific value**.

Acknowledgements & Contact

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