

BEST PRACTICES FOR THE ALZHEIMER'S DISEASE RESEARCH CENTERS

DNA /RNA / PROTEIN GUIDELINES

I. General

A. Whether prepared from biofluids or from tissue, must be collected according to local IRB and state legal codes, using appropriate informed consent forms, with adherence to HIPAA regulations^{1,2} (see Informed Consent, Confidentiality and Privacy Guideline) and NIH Genomic Data Sharing (GDS) Policy.

B. Bioanalysis for quality control (e.g., standard assays for integrity of RNA) is recommended, if funding permits, using as little of the specimen as possible.³

C. Protein is best preserved by rapid postmortem body cooling and freezing of samples up to 50 hr postmortem.⁴

II. Safety Provisions

A. Laboratories must have safety plans.

B. Laboratory personnel

- a. Immunization for hepatitis B is recommended.
- b. Must be trained in safety procedures related to handling of human tissue
- c. Must observe universal precautions; all specimens must be handled as if infectious

C. Biospecimens

a. It is recommended that a disclaimer accompany all biospecimen disbursements, even if tested negative for HIV and hepatitis B and C, which PIs sign and return to Core leaders. The disclaimer would indicate that they understand that absence of infectivity of biospecimens cannot be guaranteed, that laboratory personnel have been trained in procedures related to handling of human tissue, and that universal precautions will be observed.

b. HIV and hepatitis B and C

1. Testing of blood for hepatitis and HIV may be performed, if desired. However, as there can be both false positives and negatives, a negative test for hepatitis or HIV does not guarantee absence of infectivity. **NOTE: Good lab practice for working with any biospecimen sample is to assume that the sample is positive and should be treated accordingly.**
2. Cases with a history of hepatitis B or C or HIV infection may be excluded from brain donation unless a study specifically requires this type of tissue.
3. It is recommended that frozen brain, blood, and DNA not be distributed from cases positive for hepatitis or HIV, unless a study specifically requires this type of tissue. These may be kept and labeled as either hepatitis or HIV positive for such needs. Fixed tissue may be distributed with specific hepatitis and HIV warnings as above.

III. Annotating

It is essential that all biospecimens be de-identified and highly recommended they be given a unique identifier that follows the specimen from acquisition through processing and storage to retrieval and distribution.

IV. Storage and Retrieval

A. Storage

a. It is recommended that a portion of brain tissue be frozen and stored for biochemical and molecular/genetic studies and the remainder of the brain be fixed for preparation of paraffin blocks, etc., which are kept permanently.

b. Stabilization

1. Note: Consideration given to storage bags/containers that protect the integrity of the contents is recommended.

2. Freezers that are monitored by automated security alarm systems that contact laboratory director and personnel by telephone or pager when failure occurs are recommended.

3. Freezers with back-up systems (e.g., CO₂ or LN₂) or spare freezers for emergency situations are recommended.

c. Temperature recommendations

1. Formalin-fixed: room temperature (20-25°C)

2. Paraformaldehyde-fixed, sucrose/sodium azide preserved: refrigerator (2-8°C)

3. Frozen: -70-80°C or liquid nitrogen vapor

B. Retrieval

a. Biospecimen requests must be approved by the appropriate decision-making body (see Dissemination / Discarding Guideline).

b. Effective annotation that results in minimal effort expenditure to retrieve samples is recommended.

c. Tracking and storage methods that minimize disruption of stable state during retrieval to ensure biospecimen quality are recommended.

d. Inventory database is recommended to track specific position of each biospecimen.

e. Investigators receiving biospecimens must be warned to observe universal precautions; all specimens must be handled as if infectious.

References

1. Federal Register Department of Health and Human Services, Title 45, Code of Federal Regulations, Parts 160 and 164

2. Root J. Field guide to HIPAA implementation, rev. ed. American Medical Association Press, 2004.

3. National Biospecimen Network Blueprint, Andrew Friede, Ruth Grossman, Rachel Hunt, Rose Maria Li, and Susan Stern, eds. (Constella Group, Inc., Durham, NC, 2003); Appendix M, Advanced Analysis Techniques
4. Ferrer I, Santpere G, Arzberger T, et al. Brain protein preservation largely depends on the postmortem storage temperature: implications for study of proteins in human neurologic diseases and management of brain banks: a BrainNet Europe study. *J Neuropathol Exp Neurol* 66:35-46;2007.
5. National Cancer Institute, NCI best practices for biospecimen resources, 2011; NCI Best Practices website: <http://biospecimens.cancer.gov/practices/>; PDF of the NCI Biospecimens Best Practice: <http://biospecimens.cancer.gov/bestpractices/2011-NCIBestPractices.pdf>
6. Alzheimer Disease Genomics Sharing Plan: <https://www.nia.nih.gov/research/dn/alzheimers-disease-genomics-sharing-plan>