

National NeuroAIDS Tissue Consortium
Data Coordinating Center
INVESTIGATOR REQUEST FOR SPECIMENS

Dear Investigator:

Thank you for your inquiry about receiving human tissues or fluids (hereafter “tissues”) from the National NeuroAIDS Tissue Consortium. In order to evaluate your request, the Consortium requires that you provide the following:

- Complete the **Investigator Request for Specimens form**, including an abstract that clearly describes the project for which you will use human tissues or data. Please also include a detailed justification for the number of cases and quantity of tissue/fluids you have requested.
- Provide a copy of your curriculum vitae or NIH Biosketch.
- Provide a list of approved grant support for your research program (i.e., Federal grant number, foundation or other private support, or identify current collaboration or mentor-trainee affiliations).
- Visit <https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html#c1> to determine if your study requires a human subject research application that must be reviewed by an IRB.

Read and Sign:

- The Human Tissue Handling Risks & Safety Precautions Statement.*** This will acknowledge your responsibility in the understanding of and adherence to appropriate safety standards for the protection of yourself and other laboratory personnel under your supervision while handling human tissues.
- Human Specimen and Data Single User Agreement.*** This will acknowledge your responsibility in not distributing any portion of the tissue disbursement to colleagues or other investigators, and that all such inquires will be directed to the NNTC Director.
- The NNTC Acknowledgement Agreement.*** This will indicate that you have agreed to provide specific acknowledgment of the NNTC and its Federal grant number in any publications related to the use of these tissues.
- The NNTC Commercial Use Policy and Disclosure.*** This will acknowledge your responsibility to inform the NNTC of any potential commercial utilization of specimens provided by the Consortium.
- The NNTC Data Sharing Agreement.*** This will acknowledge your responsibility to provide the NNTC with all data within twelve (12) months of receiving materials.

All requests undergo a review process in the order received. The Data Coordinating Center (DCC) first processes this application to ensure clarity and completeness prior to broadcasting to the NNTC Allocations Committee. Please note that following this broadcast, the committee requires at least two weeks to complete their review of each tissue and/or letter of support request. Upon approval, the letter or tissue will be shipped to your laboratory as such samples become available to the Consortium. The Consortium charges no fee for providing this service. The cost of shipping, however, will be assumed by the recipient. Federal Express is the preferred courier, for which we require you provide us with your account number for charging purposes. If a different courier is preferred by you, please indicate the courier name and your account number on page 2.

Please feel free to contact us regarding the status of your request for tissue or with any other questions you may have. The Consortium is pleased to be able to provide this specialized service to help facilitate your research program.

Sincerely,
NNTC Data Coordinating Center



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I. Investigator's Information

Investigator's Name: **Phone #:**

Investigator's Title: **Dept.:**

Project Title:

Institution's Name:

Fax #:

Courier Name *(required)*:

Courier Account # *(required)*:

Investigator's Email Address:

Laboratory Shipping Address *(complete below)*:

Lab Name:

Address Line1:

Address Line2:

City/State:

Zip Code:

Country:

Name of Lab Director *(if different from above)*:

Lab Director's Email Address:

Lab Phone #:

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II. Please attach a brief summary of the project for which you are using NNTC specimens

Include in the summary:

- Specific aims and hypotheses
- Background research
- Proposed analyses
- Rationale for the number of cases and controls requested (e.g., power analyses)
- Detailed rationale for the amount of tissue/fluids requested per case

Attach additional pages as needed.

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III. Specifications for Cases and Groups Requested

The combination of fields on each line in the table below should uniquely identify your groups, including controls if needed. Inclusion and exclusion criteria listed below will be used to query the central database to find potential cases suitable for your study. To obtain the most accurate query results, please provide as much detail as possible regarding your proposed criteria for case selection.

Number of Cases	HIV Status	Pathological Dx ¹	Neurocognitive Strata ²	Age	Gender	Inclusion ³	Exclusion ³	Other

¹ **Pathological Dx:** Specify the desired neuropathological diagnosis: HIV encephalitis, PML, etc. A list of NNTC pathological diagnoses is appended below.

² **Neurocognitive Strata:** The NNTC uses an in vivo neurocognitive clinical diagnosis that is based on subject’s pre-mortem neurological and/or neuropsychological (NP) evaluation or by post-mortem review of records (if the subject could not be examined). **Note – some requests may better benefit from stratification based on a continuous measurement of cognition, rather than the clinical diagnoses described below. If your project is considering cognitive outcomes, the NNTC suggests stratifying groups by neuropsychological clinical ratings. A clinical rating of 0 to 4 is considered unimpaired while a clinical rating of 5 to 9 is considered impaired. Consultation with an NNTC neuropsychologist is available upon request to discuss utilization of cognitive outcomes appropriate to the goals of your research project.**

1. Neurocognitively Normal
 - Subject had no significant cognitive complaints, no evidence of impairment on neuropsychological testing, and/or no loss of functional capacity.
2. Asymptomatic Neurocognitive Impairment (ANI)
 - Subject had no significant cognitive complaints, but neuropsychological testing revealed evidence of mild NP abnormalities that do not impair activities associated with daily living or manifest themselves with clinical symptoms.

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3. Mild Neurocognitive Disorder (MND)
 - Subject or others report symptoms of cognitive decline; evidence of mild NP impairment; decline in functional capacity that does not reach severity required to diagnose dementia. Subject may or may not have had a diagnostic evaluation to rule out other causes of cognitive impairment.
4. HIV-Associated Dementia (HAD)
 - Subject or others report symptoms of cognitive decline; evidence of moderate or severe NP impairment on neuropsychological testing; decline in functional capacity that reaches the level of a dementia; subject may or may not have had a diagnostic evaluation to rule out other causes of neuropsychological impairment.
5. Neurocognitive Impairment Other: Probable neuropsychological impairment or dementia due to other cause.
 - Subject has impairment of some degree but there is history, physical finding, or laboratory evidence of one or more opportunistic infections (such as Toxoplasmosis encephalitis, Cryptococcal meningitis, etc.), tumors (such as Primary CNS Lymphoma), other acquired neurological diseases (such as stroke), metabolic disease (such as hepatic encephalopathy) or any other condition that would cause the impairment. A specific diagnosis is given for common AIDS-related CNS diseases.

³Inclusion/Exclusion: Specify any additional inclusion and/or exclusion criteria you wish to consider for your groups.

1. Substance Use History: PRISM/CIDI vs. Urine Toxicology, consistent history across all visits (use/abstinence) or defined history only at the last visit?
2. Co-morbidities: HCV, organ system disease, diabetes, risk factors, etc.
3. ARV and other concomitant medications: Currency of medications use relative to death, class of medications, etc.
4. Lab determinations: Viral load thresholds, nadir CD4, time frame of results relative to sample collection and/or death, etc.

Maximum time from death to autopsy:

Lab/Clinical data required:

- CD4 Count
- CSF HIV RNA
- Plasma HIV RNA
- Other:

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IV. Tissue Preparation

*Please provide a detailed outline of your specific tissue needs.

*Please note that for some diagnoses, tissue can only be distributed as it becomes available.

*Standard fluid aliquots from the NNTC are as follows:

- Plasma, CSF, and Serum = 0.5 mL
- PBMCs = 5×10^6

1. Snap frozen block -70°C (not treated with cryopreservatives)
a. Specify weight/dimensions:

2. Fixed in 10% buffered formalin

3. Paraffin sections
a. Specify thickness:
b. Number of sections:

4. Frozen cerebral spinal fluid

5. Frozen blood
a. Specify: plasma cells serum

If requesting fluid samples:

Do fluids have to come from the same case providing brain samples? Yes No

Comments:

Would you accept fluid samples collected at time points other than antemortem? Yes No

Comments:

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V. Brain Regions Requested

*Please provide a list of brain regions required for your research in order of preference.

Regions Critical For Protocol	Additional Regions If Available

Do all critical regions indicated above need to be available for every case? Yes No

Additional comments:

To assist with defining your tissue request, located below are the uniform NNTC diagnostic categories for neuropathologic evaluation of brains, spinal cords, and nerves. Please indicate any specific inclusion and/or exclusion diagnoses in the table in section III.

A. Brain

Diagnosis
1. Normal
2. Aseptic leptomeningitis (in absence of other local pathology)
3. HIV encephalitis
4. CMV encephalitis (includes ventriculoencephalitis, microglial nodule encephalitis with CMV inclusions, focal CMV necrosis)
5. Microglial nodule encephalitis, not otherwise specified (encephalitis without diagnostic inclusions or organisms)
6. Toxoplasmosis, active
7. Toxoplasmosis, healed
8. Cryptococcus
9. Progressive multifocal leukoencephalopathy
10. Lymphoma (primary and concurrent with systemic, meningeal and/or parenchymal)
11. Bacterial leptomeningitis
12. Bacterial parenchymal infection
13. Tuberculosis

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Diagnosis
14. Other infections
15. Anoxic-ischemic encephalopathy (focal or global)
16. Alzheimer type 2 astrocytosis
17. Focal (territorial) infarct (large or small, and due to embolism or local vascular pathology, recent or remote)
18. Hemorrhage, dura or leptomeninges (acute or organizing, due to any cause)
19. Hemorrhage, parenchymal
20. Other, non-infectious pathology
21. Minimal, non-diagnostic abnormalities

B. Spinal Cord/Nerve

22. Normal
23. HIV myelitis
24. CMV myelitis (includes myeloradiculopathy)
25. Vacuolar myelopathy
26. Microglial nodule myelitis, not otherwise specified
27. Toxoplasmosis
28. Cryptococcus
29. Aseptic leptomeningitis
30. Lymphoma
31. Bacterial leptomeningitis
32. Bacterial parenchymal infection
33. Tuberculosis
34. Other infections
35. Anoxic-ischemic damage
36. Hemorrhage, dura or leptomeninges
37. Hemorrhage, parenchymal
38. Peripheral neuropathy
39. Other, non-infectious pathology
40. Minimal, non-diagnostic abnormalities

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VI. Human Tissue Handling Risks and Safety Precautions Statement

Working with human tissue carries the potential risk of exposure to infectious diseases that may be communicable to other humans. All human brain tissue should be treated as a potential contamination risk for certain diseases and should be handled with extreme care. Infectious agents that have been identified as possible risks include, but may not be limited to, Human Immunodeficiency Virus (HIV-1, HIV-2), Hepatitis-B and Creutzfeldt-Jakob disease. Although a relatively rare disease entity, Creutzfeldt-Jakob disease has been reported to be able to remain infectious for long periods of time in fixed tissue and it may withstand standard autoclave sterilization procedures.

It is recommended that universal precautions be followed when working with human tissues irrespective of the method of tissue preparation. Investigators are encouraged to incorporate double gloving, appropriate protective garments, and face or eye protection when working with tissue. Disposable instruments and/or an effective regimen of appropriate decontamination should be used routinely. All waste material should be considered as a biohazard. Waste should be disposed of according to your institution's policy for handling such material, which may include incineration, autoclaving and burial, or other approved methods. All laboratory staff that will be working with human tissues should be trained in the proper and approved methods of handling of such specimens.

The NNTC collects HIV negative and HIV positive tissue specimens representative of a wide variety of additional diagnoses from across the United States. The NNTC does not guarantee that any of the donors of specimens were not exposed to or infected by potentially transmissible infectious agents. Ultimately, it is the responsibility of the recipient investigator to ensure that proper, safe handling techniques are employed by all laboratory staff in handling human tissue.

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

I have read the Human Tissue Handling Risks & Safety Precautions Statement, and I understand the potential safety risk in handling human tissue and acknowledge these safety precautions and recommendations as essential to my safety handling of specimens.

As the Investigator of Record, I accept full responsibility to ensure that proper, safe handling techniques are employed in my laboratory when working with human tissue, and further accept responsibility to train staff in approved and customary safe handling techniques before they work with these tissues.

I understand that NNTC distributes specimens known to have been exposed to or infected with agents such as, but not limited to, HIV (HIV-1, HIV-2), Hepatitis-B or Creutzfeldt-Jakob disease, and I understand that the NNTC is unable to guarantee that any of its tissue donors were not exposed or infected with such agents.



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Investigator of Record

Print Name:

Investigator of Record

Sign Name: _____

Date:



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VII. Human Specimen and Data Single User Agreement

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

As the Investigator of Record, I understand that the NNTC has disbursed human tissue, fluids, and/or data to me for research purposes only. I acknowledge that these samples and/or data have been disbursed for my express use only, that I will exercise a good faith effort to keep control over such samples/data, and that I will not distribute any samples/data or fractions of samples/data to other investigators without the express permission of the NNTC. I acknowledge that providing any amount of sample and/or data to colleagues, other investigators, or other laboratory facilities is specifically prohibited without written permission from the NNTC. I will direct all such requests for tissue and/or data to the NNTC central office. I also acknowledge that under no circumstances will the NNTC release the key that links coded private information or specimens to a specific individual.

Investigator of Record

Print Name:

Investigator of Record

Sign Name: _____

Date:



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VIII. NNTC Acknowledgment Agreement

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

As the Investigator of Record, I agree to provide specific acknowledgment of the National NeuroAIDS Tissue Consortium and its Federal grant number(s) in any publication related to the use of this tissue sample. Individual sites and the Data Coordinating Center (DCC) should be acknowledged if their resources were used in any stage of the project. If, for example, a request is submitted through the DCC for tissue and related data, and MHBB and CNTN provide tissue, the DCC and the two sites must be acknowledged. If two NNTC sites collaborate on a project and do not use the DCC resource, the two sites should be acknowledged.

“This publication was made possible from NIH funding [insert author’s funding source information]; along with shared resources from NIH funding through the NIMH and NINDS by the following grants:

- Manhattan HIV Brain Bank (MHBB): U24MH100931
- Texas NeuroAIDS Research Center (TNRC): U24MH100930
- National Neurological AIDS Bank (NNAB): U24MH100929
- California NeuroAIDS Tissue Network (CNTN): U24MH100928
- Data Coordinating Center (DCC): U24MH100925

Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the NNTC or NIH.”

I understand that no member of the NNTC staff may be listed as a co-author on any publication unless there is a substantive scientific contribution above and beyond the provision of tissue specimens. To include a NNTC staff member as a co-author, contact the DCC to obtain formal permission of the NNTC Director.

Investigator of Record

Print Name:

Investigator of Record

Sign Name: _____

Date:



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IX. NNTC Commercial Use Policy and Disclosure

Recognizing that the individual repositories constituting the NNTC must be observant of their local institutional and state regulations, the Consortium can only issue broad guidelines for commercial utilization of its specimens. The individual institutions in which the repositories reside are charged with regulatory oversight of the tissue banking operations. Individual tissue banks within the Consortium may elect to fulfill or opt out of requests entailing commercial utilization. The NNTC will neither encourage nor restrict commercial access to its specimens.

If an investigator conducting research with NNTC specimens previously distributed under a not-for-profit application, wishes to switch their utilization to commercial use, he or she must re-submit an application to the NNTC requesting permission for this switch. At that time, participating repositories will be given the option of either granting or denying permission for such utilization.

Please answer the following question:

Will the specimens you receive from the NNTC be used for any commercial purposes? Yes No

Comment:

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

As the Investigator of Record, I understand and agree to the terms specified in the NNTC Commercial Use Policy. I also agree that my disclosure of commercial interests has been accurately reported on this application. If at some point, however, your commercial use status changes, I will promptly inform the members of the NNTC.

Investigator of Record

Print Name:

Investigator of Record

Sign Name: _____

Date:

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X. NNTC Data Sharing Policy

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

The NIH [National Institute of Mental Health (NIMH) and The National Institute of Neurological Disorders and Stroke (NINDS)] sponsors this enterprise through cooperative agreements with the brain banking units. The NNTC Data Coordinating Center (DCC) coordinates, stores, and makes accessible all de-identified data obtained from the NNTC subjects and specimens derived from the subjects. As a recipient of data from the NNTC you agree to the following statements:

- The NIH expects NNTC recipients to provide the DCC with electronic copies of all data within twelve (12) months of receiving the materials. If this is not possible the DCC will work with the investigator to decide on an appropriate time-frame.
- Continued reporting to the DCC should occur at least annually as the analysis progresses until the analysis is completed.
- Data can be embargoed to prevent its release until publication. All data will be referenced to the investigator and publication when relevant.
- For indexing purposes the NNTC expects recipients to submit data in a specific format with an NNTC subject ID number; forms for this submission will be provided upon approval of the resource request.
- High-throughput data (genomic, gene expression, protein and metabolomics data) should be submitted to the appropriate NCBI repository (dbGap {<http://www.ncbi.nlm.nih.gov/gap>} for genomic, GEO {<http://www.ncbi.nlm.nih.gov/geo>} for gene expression, other data types if/as they become available), using their respective formats and the appropriate links provided to the DCC. Other high-throughput as well as medium- and low-throughput datasets and associated metadata are to be submitted to the DCC; working with the DCC to determine the best format to transfer data.
- Some data may be missing from the NNTC central database. The NNTC will attempt to provide investigators with the most up-to-date data tables. On a periodic basis, the DCC will freeze the database to create files for public distribution. The tables are subject to revision through a process of quality assurance monitoring, both centrally and locally at each site.
- Data returned to the NNTC may be shared with qualified requestors. Requestors will be notified if another investigator has received access to their submitted data.



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I understand that the NNTC intends to make these data available for qualified scientific investigators.

Investigator of Record:

Print Name:

Investigator of Record:

Sign Name: _____

Date:

PLEASE MAIL OR FAX COMPLETED FORMS TO:

National NeuroAIDS Tissue Consortium
Data Coordinating Center
Request Manager
401 N. Washington Street
Suite 700
Rockville, MD 20850
Tel: 1-866-NNTC-BRAIN
Fax: 301-576-4597
Email: nntc@emmes.com