NSW BRAIN BANKS (NSWBB)

Incorporating the Sydney Brain Bank (SBB) and NSW Brain Tissue Resource Centre (NSW BTRC)

Guidelines for Researchers

“Annexure 1”

Updated March 2018
Introduction

The Sydney Brain Bank (SBB) located at Neuroscience Research Australia (NeuRA) and the NSW Brain Tissue Resource Centre (NSW BTRC) located at the University of Sydney have coordinated programs and banking procedures to operate together as the NSW Brain Banks (NSWBB). Our aim is to provide Australian and international researchers with access to well characterised post-mortem human central nervous system tissue through an integrated process.

Cases Available

Only tissue from adult subjects (aged 18+ years) is collected. Material currently collected by the NSWBB includes cases with dementia, movement disorders, neuropsychiatric and alcohol-related disorders, as well as normal controls. These cases are recruited through a number of prospective brain donor programs and from the NSW Department of Forensic Medicine. Further information about the donor programs can be found on our website: https://nswbrainbank.org.au/donors/brain_donor_programs. All cases are clinically and pathologically characterised. The tissue is suitable for genomic, neuroanatomical, neuropathological, neuropharmacological and neurochemical studies.

Accessing Tissue from the NSWBB

Initial enquiry

Researchers may submit an enquiry regarding their tissue requirements through the NSWBB tissue request website at https://nswbrainbank.org.au/researchers/tissue_request. A tissue manager will assess each enquiry and ascertain the availability of tissue. Researchers will be advised if there are any issues with tissue supply. If the enquiry is feasible the researcher will be made aware of the NSWBB policy on cost recovery and the need for a Tissue Transfer Agreement (TTA) to be signed following approval of a tissue request (see Cost recovery and Tissue Transfer Agreements below). Once these items have been discussed and agreed by the researcher, a tissue application form will be made available for completion online. Please ensure the Principal Investigator submits the application, as only the initiating individual will have access to the online application. The Principal Investigator should be the person responsible for the study. They will be required to sign the TTA and will be invoiced for any cost recovery. For student projects, the supervisor or post-doctoral researcher responsible for the research project should submit the application. The Principal Investigator will need to submit a biosketch, which will be used to assess their expertise and ability to undertake the research.
Other options are available at the enquiry phase:

1. Provision of a letter of support to confirm availability of tissue for granting bodies or Institutional Human Research Ethics Committees. An estimate of cost recovery will be included in this letter (see Cost recovery below).

2. Provision of limited ‘trial’ tissue for the purpose of developing new techniques or gaining preliminary data for power analyses. This tissue is from cases that have not met diagnostic criteria but are still suitable for this purpose. Requests for trial tissue require timely feedback to the NSWBB on outcomes and are expected to progress to a full tissue application if the trial is successful. It would not be expected that data from trial tissue would be suitable for publication. See also Pilot studies section below

Application process

Once an online application is initiated, the Principal Investigator must complete all sections of the application, as follows:

- **Principal Investigator and all Co-Investigator details.** All people involved in the project, including students, must be named on the application. *Please note that a student is not eligible to act as Principal Investigator on any application.*

- **Biosketch of Principal Investigator,** including summary of positions held, key publications, research expertise and project keywords (these details may be entered by completing the My Profile section online).

- **Project details,** including funding details and start/completion dates of project.

- **Tissue requirements,** including the case information required as justified in the application. Before completing your application, please ensure you have read the Guidelines for Experimental Design and Assessment, which can be downloaded from the NSWBB website (https://nswbrainbank.org.au/researchers/tissue_request).

Important considerations when requesting tissue for your study:

- the total number of cases required for the statistical analysis is justified in the application. It is highly recommended that a power analysis based on reasonable assumptions is included in the justification, otherwise it will be difficult for assessors to determine the feasibility of the study. Examples of power analyses are provided in the Guidelines for Experimental Design and Assessment to assist with your study design and justification. Requests for
smaller numbers of cases to carry out an initial pilot study can be made but should also be justified (see Pilot Studies below).

- the type/s of tissue requested and justified in the application i.e fresh-frozen, formalin fixed, paraffin-embedded sections
- region/s of the brain required for study, as justified in the application
- the amount of tissue requested with justification of the weight or number of sections based on preliminary work (e.g. yields of extracts protein, RNA; number of stains)

Please note: the type and amount of tissue requested must accurately reflect what is required to complete the project using the statistical methodology described. Requests for larger amounts of tissue will not be filled.

Research summary, including an uploaded project outline and justification of the tissue requirements. Please use the NSWBB project outline template to complete your project outline. This can be downloaded from the following address: https://nswbrainbank.org.au/researchers/tissue_request. Please ensure you complete all relevant sections of the application. Incomplete applications cannot be processed. If the research is a significant part of a peer reviewed and funded project grant, providing the 1-2 page summary of the grant application with the tissue request will expedite the review process. Projects forming part of a successful program or fellowship grant cannot be considered for expedited review as specific project details and research methods are not outlined in these applications.

- Proof of ethics approval for the project. All people involved in the project, including students, must be named on the ethics approval. Applications for tissue will not be considered unless accompanied by appropriate ethics approval or an institutional letter stating that approval is not required.

Assistance can be sought at any time via the online messaging system if there are any problems with the application process.

Case information available for researchers

The information available to investigators includes age, gender, disease duration, cause of death, post-mortem delay, fresh tissue pH and neuropathological disease classification. Any additional clinical information remains the intellectual property of the recruiting brain donor program or brain bank. Researchers requesting additional clinical
information will be referred to the co-ordinator of the recruiting brain donor program/s to obtain approval to access this information. The tissue request will not be considered further until this approval is granted. Where clinical information is provided, the recruiting brain donor program may negotiate authorship with the Principal Investigator. Similarly, if additional pathological information (e.g. disease staging) is required this will be subject to negotiation and approval from the NSWBB and may require authorship.

**Pilot studies**

Researchers may request tissue for the purpose of carrying out an initial pilot study as part of a two-stage study design. The approval for a pilot study differs from approval for trial tissue to be used for technical and/or statistical purposes, with pilot study approval given by the NSWBB Scientific Review Committee (SRC, see review process below) only following approval of the full two-staged project in its entirety. The scientific rationale, aims and hypothesis of the full two-staged project must be provided and justification concerning the need for an initial pilot study must be included in the project outline. Please use the NSWBB project outline template, which can download from: [https://nswbrainbank.org.au/researchers/tissue_request](https://nswbrainbank.org.au/researchers/tissue_request).

If no research outcomes are forthcoming from the initial pilot study in the timeframes agreed on, the researcher will be asked to provide reasons for the lack of outcomes in their annual evaluation review. Any requests for further tissue to complete the study will be considered as a new application.

Where necessary, the SRC may also request a two-stage study design with an initial pilot study prior to supplying tissue requested for a full study.

**Review process and timing**

The review process is confidential and each tissue request takes approximately 4 weeks to be processed. However, this can take longer at busy times (e.g. Feb-May when many student projects start) or if the review process identifies that additional information is required.

Two review committees are associated with assessing the tissue applications from researchers - The NIAAA Scientific Advisory Board reviews requests from researchers for studies of alcohol-related brain damage and the NSWBB SRC assesses all other applications. For applications assessed by the SRC, institutionally-appointed academic members assign reviewers from the NSWBB Tissue Review Panel (TRP) to assist them with their final decision to the SRC Chair. Both the SRC academics and TRP members are
independent researchers with expertise in the field of neuroscience and tissue-based research. All assessments are performed confidentially and independently of brain bank staff. The independent Chair of the SRC ratifies the final recommendation of the SRC members in order to ensure objective and thorough review of all applications. Only meritorious research projects will be approved.

**Tissue Transfer Agreements and timing**

All researchers involved in the project and their institution must sign a TTA prior to the supply of tissue. The NSWBB have a combined TTA available when tissue is supplied by both brain banks. If the project requires tissue and/or progeny to be sent to investigator/s at other institution/s (details of which must be provided in the tissue application), an adhesion agreement must also be signed. The time taken to sign the TTA is dependent on processes in the recipient institution.

**Tissue supply, cost recovery and courier costs**

Tissue will be supplied to researchers in as short a timeframe as possible, but may take longer if the tissue request is large or at times of peak demand. A tissue manager will advise if there will be any delays to tissue supply following receipt of the completed TTA. Australian law clearly prohibits the sale of human tissues. However, cost recovery is necessary to offset the considerable operational expenditure by the NSWBB associated with the personnel and consumables necessary to collect, process, characterise, and store the tissue, as well as the data management and quality assurance systems required. Access rates for these services are in accordance with a National Access Policy (available on request). Please contact us to obtain an estimate of cost recovery prior to submitting any grant application to fund a project requiring human brain tissue from the NSWBB (or request a letter of support online).

Following the approval of a two staged study by the SRC (pilot followed by second part of study), the tissue will be given separately for the initial pilot study versus the second part of the study to complete the project, and with negotiation the applicant given an appropriate, project-specific timeframe to carry out the first stage pilot study. The supply of further tissue for the second part of the study to complete the project is dependent on the outcome of the initial pilot study, and the applicant is expected to submit a request for the remaining cases to the NSWBB Amendment Review Panel (AP, see amendment section below) for review in the agreed timeframe. The results of the initial pilot study and full details of the entire project, including how it might differ from the original application, must be provided. If approved by the AP (see amendment section below), the tissue for the
second part of the study to complete the project will be supplied with an adhesion agreement to the original TTA. Time extensions for initial pilot studies may be requested through the AP with appropriate reasons.

All courier charges are the responsibility of the requesting researcher and should also be included as a budget item in any grant application requiring human brain tissue from the NSWBB. The Principal Investigator and their institution are also responsible for complying with appropriate customs and other regulations for the transportation and importation of human tissue within or from Australia. The Principal Investigator is also responsible for any transport costs associated with returning unused tissue to the NSWBB.

**Use of tissue and amendments to approved projects**

The tissue, including any progeny and unmodified derivatives (see definitions below) must only be used for the project described in the application. It must not be used for any other project, or be passed to any third party who is not named on the tissue request. Any proposed modification to an approved project must be formally assessed by the AP and decisions ratified by the independent Chair of the SRC. An amendment to the original request may be submitted via the online system where researchers wish to:

a) Notify the NSWBB about the addition of other researchers or when an investigator who is using the tissue moves to a different institution (note that adhesion agreement/s to the existing TTA will be required if the researcher is from a different institution);

b) Request additional tissue for studies that are within the scientific scope and aims of the original application and are necessary for completion and publication of the original study. A new tissue request may be required if additional anatomical regions or cohorts with a different disease classification are requested;

c) Request permission to use remaining tissue, including any progeny and unmodified derivatives for purposes other than those described in the original application. A new TTA will be required.

If you are unsure about whether your application fits the amendment criteria, please contact the NSWBB. If the original project was approved more than 5 years prior, or if 3 or more amendments relating to the use of tissue have already been submitted (there is no limit to amendments relating to changes in personnel), please discuss the application with the NSWBB prior to submission. Any other modifications to the original requests should be discussed with the NSWBB.
Safety

The NSWBB is aware of the dangers and risks to researchers from potentially infectious human material. Within the NSWBB, the tissue is handled according to Institutional Work Health and Safety guidelines. While every effort is made to exclude infectious cases, we cannot guarantee that cases are not infectious. **We would like to highlight the importance of handling human brain tissue as if it is potentially infectious at all times.** Researchers accessing the tissue from the NSWBB should comply with handling procedures of their institution(s). It is the Principal Investigators’ responsibility to ensure that adequate safety information and necessary training are provided before co-investigators (including students) can use the tissue. It is recommended that any person working with human tissue have hepatitis immune status verified and undergo vaccination if necessary.

Acknowledgements

Researchers must acknowledge the brain bank/s in all oral and written presentations and publications resulting from use of the tissue and/or progeny. Failure to comply with this requirement will jeopardise future access to NSWBB tissues. Wording of the required acknowledgements will be provided in the TTA.

Examples of acknowledgements;

“**Tissues were received from the New South Wales Brain Tissue Resource Centre at the University of Sydney supported by the Schizophrenia Research Institute and the National Institute of Alcohol Abuse and Alcoholism (NIAAA)”**

“**Tissues were received from the Sydney Brain Bank which is supported by Neuroscience Research Australia and the University of New South Wales.”**

NIH Access Policy

Publications that have used tissue from the NSW Brain Tissue Resource Centre are required to comply with the NIH Access Policy. The Recipient agrees, following the acceptance of a paper for publication, to promptly submit a copy of the final peer-reviewed paper to the digital archive PubMed Central. The Recipient will ensure that all publishing agreements for such papers signed by Recipient and/or Recipient Personnel allows for the paper to be posted to PubMed Central in accordance with the NIH Public Access Policy found at: http://www.ncbi.nlm.nih.gov/pmc/.

Reporting requirements

Principal Investigators must provide an annual report on the progress and outcomes of the project. These reports must identify all presentations and publications.
arising from the use of the materials. Annual reports are required until completion of the project and all research outcomes have been published.

Audits will be performed annually to identify users who do not return their evaluations and closed projects with no research outputs. Users may be blocked from accessing the resource if evaluations and research outcomes are not forthcoming.

**Participating in the review process**

The NSWBB requires that all investigators named on the application, other than students, act as confidential TRP reviewers for future NSWBB tissue requests. Reviewer details, including title, name, position, contact details and keywords describing the research area and methodological expertise (3-5 keywords for each), provided in the tissue request, will be held in a database for the purpose of identifying appropriate reviewers. The NSWBB SRC identify at least 2 TRP reviewers for each application and reviewers must submit their anonymous confidential review within one week of acceptance. Before submitting your review, you will be asked if you agree to your anonymous confidential review being shared with the applicant and the other reviewers. Only the SRC members and the SRC secretary will know the identity of the reviewers. The SRC reserves the right to remove any ill-informed remarks or perjorative comments from any review prior to anonymous sharing.

**Abbreviations**

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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>NeuRA</td>
<td>Neuroscience Research Australia</td>
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<tr>
<td>NIAAA</td>
<td>National Institute for Alcohol Abuse and Alcoholism (USA)</td>
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<td>NSWBB</td>
<td>NSW Brain Banks</td>
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<td>NSWBB SRC</td>
<td>NSW Brain Banks Scientific Review Committee</td>
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<td>NSW BTRC</td>
<td>New South Wales Brain Tissue Resource Centre</td>
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<td>SBB</td>
<td>Sydney Brain Bank</td>
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<td>TTA</td>
<td>Tissue Transfer Agreement</td>
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**Definitions:**

- **Modifications** means any substances created by the Recipient through use of the Tissue which contain or incorporate the Tissue.
- **Progeny** means an unmodified descendant from the Tissue, such as virus from virus, cell from cell, organism from organism.
- **Unmodified Derivatives** means substances created by Recipient which constitute an unmodified functional sub-unit or an expression product of the Tissue, for example: sub-clones of unmodified cell lines; purified or fractionated sub-sets of the Tissue; proteins expressed from DNA and/or RNA; DNA or RNA supplied by Provider; polyclonal and/or monoclonal antibodies secreted by a hybridoma cell lines; or sub-sets of the Tissue such as novel plasmids or vectors.
- **Third Party** – any persons not named on the tissue request or amendment.
Contact details

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