BRAIN UK

UK Brain Archive Information Network

POLICY FOR ACCESS TO TISSUE ARCHIVAL HOLDINGS OF PARTICIPATING CENTRES

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1. Introduction

The application process for research access to tissue archives held and maintained by those centres participating in the *BRAIN UK* initiative is an important mechanism that allows stakeholders to gain an understanding of the purposes for which individuals and organisations are using the service provided, how frequently and in what volume. It also enables records to be generated and maintained which can better serve to target the resources on offer and to provide evidence of audit trails should they be required at a future date.

2. Aims and Objectives

This policy sets out the process that researchers will undertake to apply for access to the tissue archives maintained by those centres participating in the *BRAIN UK* initiative and the methods by which these centres, as well as a centralised *BRAIN UK* Committee, will determine if access is to be provided and the terms and conditions relating to such access. This policy also aims to provide a guidance framework to enable these decisions to be reached in a wholly consistent and reproducible manner.

An anonymised dataset summarising the neuropathological tissue archives held by participating centres that have been removed and stored as part of a post mortem examination will be made available to the research community in an electronic format. This database will be hosted by the University of Southampton (http://www.brain-uk.org/) but will use the website of the British Neuropathological Society (BNS) (http:/bns.org.uk/) as an additional portal.

3. Application Procedure

3.1 Identification of Research Tissue Requirements

All applications will be administered centrally through *BRAIN UK* with relevant documentation being disseminated to tissue holding centres for their approval. Only applications that follow the procedure set out below will be considered as valid.

The current model employed by *BRAIN UK* is that informal enquiries are received from the research community centrally by telephone or, more commonly, via e-mail (brainuk@soton.ac.uk). After interrogation of the *BRAIN UK* linked-anonymised database information is fed back regarding the potential availability of tissue(s) and a formal application is invited if appropriate.

However, it is intended that as resources allow the *BRAIN UK* database will be made available in a fully anonymised and abbreviated form to all browsers to comply with the spirit of the Data Protection Act 1998. Functionality will be incorporated to enable searches to be performed to reveal the types of disease entity represented, the tissue format(s) available, the number of cases available (also stratified by sex), the age range and the number of participating centres holding defined tissue. The ability to perform query searches will also be incorporated to allow patient sex and user defined age ranges to be determined. Multiple searches will be permitted with all results being collated for display. A typical, but stylised, search result is exemplified below:

Diagnosis	SNOMED	Format	Cases	Male	Female	Age Range	Centres
PML	22255007	FFPE (standard)	46	27	19	52-88 years	8
PML	22255007	FFPE (oversize)	18	8	10	56-86 years	3
PML	22255007	Wet tissue	11	6	5	61-84 years	3

This format will enable researchers to identify if sufficient material is available for their requirements and stratification by sex and age range will also permit identification of relevant

material if these variables are likely to be important to their research undertakings. It will also be possible to identify pathologically normal tissue for use as control material and different tissue formats that may be suited to certain investigative techniques.

Once an individual researcher has identified that tissue of interest exists in the quantities and formats of use to them they are in a position to apply for access to tissues held by those participating centres holding such relevant material in their diagnostic archives. Applications will be made using a standardised application form which will be available electronically. Once completed, an electronic copy and a signed paper copy are submitted, along with other supporting documentation, via a centralised managed system to enable *BRAIN UK* and the relevant participating centres to reach a decision upon the validity of each application.

Future accessibility on the website to the BRAIN UK database itself for the research community will be developed in concert with specialist oversight by iSolutions within the University of Southampton.

3.2 Tissue Request Form

The current version of the BRAIN UK *Tissue Request Form is provided in the Appendix to this document.*

The application form will gather information from each research applicant and will consist of the following:

1. Principal Investigator contact details (contact name, telephone number, fax number, e-mail address, full postal address),

2. Details of where research will be taking place,

3. Shipping and invoicing information,

4. Details of proposed research study including:

    a. evidence of peer review (if applicable),
    b. evidence of ethical approval (if applicable),
    c. study protocol,
    d. funding information.

5. Details of material required from the *BRAIN UK* network of participating centres (diagnostic category, SNOMED number where known, tissue format required, patient sex, patient age range and quantity of material required),

BRAIN UK is applying for 'generic ethical approval' for the use of relevant material held by each participating centre and *BRAIN UK*, and the participating centres providing material, will need to be satisfied that all research is of sufficient quality before releasing material. A list of criteria and conditions that would need to be satisfied has been provided by the UK REC granting permission for our previous applications (Refs: 09/H0504/68 and 11/SC/0395). Under certain circumstances, additional ethical approval may be required in support of any application and this will be assessed on a case-by-case-basis (see Section 3.3 below). If 'generic ethical approval' is not forthcoming as part of this application then evidence of ethical approval from a UK Research Ethics Committee (or equivalent for applications outside of the UK) will need to be submitted in support of any application.

All original documentation forwarded to *BRAIN UK* in support of an application will be copied and returned to each applicant within 28 days of receipt unless received in an electronic format. Such information will be held confidentially by *BRAIN UK* for a minimum period of five years for the purposes of annual reports and audit.

3.3 Mechanism for Determining Approval

Once a signed application and all supporting documentation have been received by *BRAIN UK* the application will be logged and assigned a unique study number. This will enable each application to be tracked and for a record to be maintained on a database detailing which materials have been forwarded from which participating centre and to whom.

The relevant paperwork will be disseminated to the *BRAIN UK* Director responsible for the review of applications for their opinion as to whether the proposed research fulfils defined acceptance criteria.

3.3.1 Study Proposal Review

The *BRAIN UK* Director (or in his absence his deputy) will consider each application independently and will apply the same consistent criteria to aid in the decision making process:

1. The research project should be within the fields of medical or biomedical research as described on the approved Tissue Request Form and accompanying study protocol.

2. There should be evidence that the research has been subjected to a rigorous scientific critique and peer review and is appropriately designed in relation to its objectives and (with the exception of student research below doctoral level) should add something useful to existing knowledge.

3. All samples provided and any associated clinical information must be non-identifiable to the researcher at the point of release (*i.e.* anonymised or linked anonymised). The degree of anonymisation will be dependent upon the nature of the proposed research study.

4. No researcher shall be permitted to gather additional data from the living relatives of donors in the case of post mortem tissue, or from the donors themselves in the case of biopsied samples, unless this is confined to additional ethically approved arrangements for the feedback of clinically important information.

5. Supply agreements must be in place with the researcher to ensure storage, use and disposal of the samples in accordance with the HTA Codes of Practice, the terms of the ethical approval and any other conditions required by the participating centre supplying relevant material.

Assuming the granting of 'generic ethical approval' a research project in the UK using tissue facilitated by *BRAIN UK* in accordance with these conditions will be considered to have ethical approval from the Committee under the terms of this approval *if granted*. In England, Wales and Northern Ireland this means that the researcher will not require a licence from the Human Tissue Authority for storage of the tissue for the duration of this project[1].

BRAIN UK may require any researcher to seek specific ethical approval for their project under certain circumstances (*e.g.* where research is likely to generate clinically significant data or where access to living relatives is required). Such applications should normally be made to the REC granting generic approval and should be booked via the Central Allocation System.

N.B. If 'generic ethical approval' is not granted to *BRAIN UK* for the use of archived tissues held at participating centres then evidence of a favourable opinion for a research study from a UK Research Ethics Committee must accompany every application. In addition, all research must also gain the necessary approvals from the Research and Development department within each NHS Trust providing tissue for such a purpose and attainment of such approvals are the sole responsibility of the researcher.

Once an application has been accepted, relevant documentation will be forwarded to a responsible representative of each participating centre (*e.g.* a lead Neuropathologist) for them

to be informed of the proposed study and for them to formulate an opinion regarding the validity of each study and whether to make their tissue archives available.

It is important to note that each participating centre has the ultimate right to veto the access to and subsequent use of their tissue archives for any particular study proposal <u>regardless</u> of the decision of the *BRAIN UK* Director.

3.3.2 Review Timeframe

A definitive decision should be forwarded to each applicant of the final decision of *BRAIN UK* within 28 days of the receipt of the completed Tissue Application Form, signed declaration and all requested supporting documentation. However, due to unforeseen circumstances or requests for additional information, this timeframe may be subjected to unavoidable delays.

3.3.3 BRAIN UK *Committee*

This body is composed of the following individuals:

- *BRAIN UK* Director (Prof. James A R Nicoll)
- *BRAIN UK Deputy Director* (Dr David Hilton)
- Chair of the BNS Academic Committee (or their nominated representative, currently Prof. Sebastian Brandner)
- Participating Centre Representative (Dr William Stewart, Glasgow)
- Brain Tumour Bank Network Lead (Dr Kathreena Kurian, Bristol)
- A clinician with expertise in neurological research (Prof. John Zajicek)
- A basic scientist with expertise in neurological research (Dr Stephen Gentleman)
- Lay individuals (Dagmar Turner and Paul Saunders)
- Representative of *brainstrust* (Dr Helen Bulbeck)
- *BRAIN UK* Co-ordinator (Dr Clare Mitchell)

The Committee will meet twice a year to review the work of *BRAIN UK* and to formulate annual reports for dissemination to the BNS Academic Committee and the relevant Research Ethics Committee. The Committee will also be in contact with the BNS Academic Committee on a consultancy basis if it is felt that advice or guidance is required in relation to any particular application.

Prior to each meeting the Minutes from the previous meeting will be sent to all Participating Centres in order to canvass for items for discussion. Feedback from Committee members and Participating Centres will be used to formulate an Agenda for discussion.

3.3.4 Unsuccessful Applications

Those applications that do not meet the approval standards of the *BRAIN UK* review Committee will not be permitted to gain access to the tissue archives maintained by participating centres through the centralised *BRAIN UK* model. Such applicants will be informed in writing detailing the reasons for rejection. Such applications will be offered advice to enable re-submissions to be tabled should this be deemed appropriate.

All electronic and paper records pertaining will be maintained for a period of five years for the purposes of audit after which they will be destroyed. These records will be maintained securely

and will not be used for any other purpose nor passed onto third parties in accordance with the Data Protection Act 1998.

3.3.5 Successful Applications

Those applicants who have been successful will be informed in writing of such a decision. The letter of invitation (an example is included in the Appendix) will also detail the types of material they have requested and the contact details of those participating centres that would be in a position to provide such material. Each participating centre that can also potentially provide tissue will be informed of the *BRAIN UK* Director's decision and they will be forwarded the researcher's contact details. Each relevant participating centre will be informed of what cases are to be required by a particular researcher and such cases will be identified by their laboratory number or equivalent.

Arrangements concerning the format in which tissue is to be supplied (*e.g.* formalin-fixed paraffin-embedded blocks versus slide-mounted unstained sections) will be the prerogative of each participating centre. In addition, shipping arrangements and the return of unused material should also be agreed and ideally formally included in a Material Transfer Agreement (a template MTA is included in the Appendix). Funding to cover the retrieval, processing and transport of tissue will be recouped from each researcher's funding and this, as well as any other pertinent arrangements, should form part of an application for any necessary local R&D approvals which are the sole responsibility of the researcher.

Although not explicitly involved in the transfer of tissue or funds relating to applications, *BRAIN UK* will be available to facilitate the flow of resources and information should this become required.

Successful applicants will be expected to complete an annual report of progress and inform *BRAIN UK* of any incidents in relation to the use of tissue in the study (a template Annual Report form is included in the Appendix).

A flowchart summarising these processes is included as an Appendix to this document.

3.4 Applications from Outside the UK

From applications we have approved to date and from enquiries we have received it is anticipated that a proportion of applications will originate from outside of the UK which will, by definition, place such research outside of scope of the Human Tissue Act 2004 and UK Research Ethics Committees. In order for an overseas application to be considered valid researchers will have to provide evidence that they have local Ethical Approval to undertake research on human tissue and a declaration that they will adhere to local laws, policies and regulations in relation to the use, storage and disposal of tissue used for research. In addition, overseas applicants will be required to submit the common core documents as required for all applications. An obligation to adhere to these principles forms part of the Terms and Conditions which are signed against as part of the completion of the Tissue Request Form.

4. Maintenance of Records

BRAIN UK will maintain a central record of all research projects to which tissue has been supplied. The following dataset shall be maintained:

1. Full title of each project,
2. The name of the Chief Investigator,
3. The name of the Sponsor,
4. The location of the research,
5. The date of approval by *BRAIN UK*,

6. End date of the research (if known),

7. Details of all tissues released,

8. Details of all tissues returned,

9. Any relevant reference numbers.

This information will be maintained for the purposes of audit and to enable Annual Reports to be drafted for supply to the REC granting ethical approval for the *BRAIN UK* bank and to the BNS Academic Committee. Such information will be maintained securely electronically on a dedicated encrypted computer and any paper records generated will also be maintained in a secure environment and in accordance with The Data Protection Act 1998.

4.1 Audit and Annual Reporting

Audit is an important mechanism to help to determine if researchers are utilising tissues obtained from *BRAIN UK* participating centres appropriately and in line with the purposes defined within their applications. This will be partially achieved through researchers making available the results of their work through papers submitted to peer-reviewed journals and abstracts to the *BRAIN UK* Committee and by those participating centres providing information upon the issue and return of supplied tissue used in such work. As part of the auditing process it *may* also become necessary to undertake site visits to ensure that researchers are utilising tissue for the purposes defined within their applications. As a consequence, it is important that all researchers maintain adequate records of the receipt, use and return of all tissues to enable audit trails to be demonstrable.

5. Data Protection Act 1998

5.1 Data Protection Principles

BRAIN UK is committed to abide by the not only the letter but also the spirit of the Data Protection Act 1998 (the 'Act') and to promote the highest possible standards of conduct mandated by the Act. **It is important to note that a component of the *BRAIN UK* database will be using data derived from the deceased and that, in law, the Act does not apply in this instance. However, *BRAIN UK* will still adopt principles that abide by the spirit of the Act in this instance as well as mandatory obligations set out in law relating to living individuals to ensure a consistent approach is adopted and maintained**.

The Act sets out eight Data Protection Principles which are as follows:

I. Personal data shall be processed fairly and lawfully,

II. Personal data shall be obtained only for one or more specified and lawful purposes, and shall not be further processed in any manner incompatible with that purpose or those purposes,

III. Personal data shall be adequate, relevant and not excessive in relation to the purpose or purposes for which they are processed,

IV. Personal data shall be accurate and, where necessary, kept up to date,

V. Personal data processed for any purpose or purposes shall not be kept for longer than is necessary for that purpose or those purposes,

VI. Personal data shall be processed in accordance with the rights of data subjects under the Act,

VII. Appropriate technical and organisational measures will be undertaken against unauthorised or unlawful processing of personal data and against accidental loss or destruction of, or damage to, personal data,

VIII. Personal data shall not be transferred to a country or territory outside the European Economic Area unless that country or area ensures an adequate level of protection for the rights and freedoms of data subjects in relation to the processing of personal data.

5.2 Acquisition of Personal Data (Principles I, II and III)

BRAIN UK will adhere to and comply with guidelines issued by the University of Southampton's Data Protection Officer and will:

- Inform applicants of the purposes for which data is being gathered,
- Obtain the explicit consent of applicants,
- Inform applicants that the University of Southampton will be the data controller for the purposes of the Act,
- Reveal the identities of any other persons to whom the data may be disclosed.

No more data than is necessary will be collected in relation to the construction of an anonymised *BRAIN UK* database or in fairly determining the suitability of applicant researchers for access to the tissue archives maintained by participating centres.

5.3 Holding, Safeguarding and Disposal of personal data (Principles IV, V and VII)

Data will be held for the duration of approved research projects and will be maintained to enable the undertaking of audit should this become a requirement for a period of five years. A minimum data set will be kept for the purposes of the drafting of Annual Reports which will be a condition of the ethical approval of the *BRAIN UK* model.

Data will be reviewed on an annual basis to ensure that it is kept up to date and to determine if retention is still necessary.

In order to protect data and to prevent its loss, destruction or unauthorised disclosure, a number of physical, electronic and procedural safeguards will be implemented for both the *BRAIN UK* database and personal data accrued as part of the application process. These are found in detail in the accompanying document (*SOP 2: Data Security Policy*).

5.4 Processing of Personal Data (Principles I and II)

A defined dataset will be obtained for the purposes of creating and maintaining the linked anonymised *BRAIN UK* database. This will only be amended should it be required to enable the correct formatting of the database to permit it to be accessed via the internet. Once established, functionality built into the online search functions will permit the extraction of certain anonymised data for the purposes of identifying and defining tissue subsets available for research purposes.

Personal data accrued as part of the application process will be stored securely in paper and electronic form. Personal details (such as researcher names and contact details) will be entered onto, and maintained within, a secure electronic database.

5.5 Disclosures and Transfers of Personal Data (Principles I, II, VII and VIII)

Disclosure of information relating to deceased individuals will be performed using an anonymised format and in line with the policies of the University of Southampton. There will also be no transfer of personal information pertaining to any living individual outside of the University without initial recourse to the Data Protection Officer and their subsequent permission.

As information is to be made available via the World Wide Web and to ensure that Principal VIII is satisfied, data will only be made available in an anonymised format.

5.6 Destruction of Personal Data

Personal data will be maintained for as long as is necessary (as set out in paragraph 5.2) and that data earmarked for destruction shall be disposed off in a manner that ensures that the data cannot be reconstructed and processed by third parties. Methods of data destruction are covered in the accompanying document (*SOP 2: Data Security Policy*).

5.7 Data Subjects' Right of Access

Access by data subjects to any personal data held by the University will be facilitated in accordance to the University of Southampton's Data Protection Policy.

6. References

1. Human Tissue Authority (September 2009) Code of Practice 9: Research http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/codesofpractice/code9research.cfm?faArea1=customwidgets.content_view_1&cit_id=757

7. Supporting Documentation

1. Tissue Request Form

Tissue Request Forme.doc

2. Template Material Transfer Agreement

Human tissue MTA template (Rev May 09) 040214 v1_0.pdf

3. Application and Audit Process Flow Diagram

Application flowchart 040214 v1.0.pdf

4. Terms and Conditions

Terms and Conditions 040214 v1_0.pdf

5. Sample *BRAIN UK* Acceptance Letter

Acceptance Letter Template 040214 v1_0.pdf

6. Annual Review Form

Annual Review Form 040214 v1_0.pdf