

UK Brain Archive and Information Network (*BRAIN UK*)

Existing Holdings

PROTOCOL

Version 1.8

FINAL DRAFT

Author:

Name Mr Neil Bailey

Signature

Date 27th March 2009

Authorised by:

Name Prof. James A R Nicoll

Signature

Date 27th March 2009.

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1. Title

United Kingdom Brain Archive and Information Network (*BRAIN UK*)

2. Chief Investigators

Professor James Nicoll

*Professor of Neuropathology
University of Southampton
Honorary Consultant in Neuropathology
Southampton University Hospitals NHS Trust*

Mailpoint 813
University of Southampton
South Academic Block
Southampton General Hospital
Tremona Road
Southampton
SO16 6YD

Tel: 023 8079 8922
e-mail: J.Nicoll@soton.ac.uk

Dr David Hilton

*Consultant in Neuropathology
Plymouth Hospitals NHS Trust*

Derriford Hospital
Derriford Road
Crownhill
Plymouth
PL6 8DH

Tel: 01752 763599
e-mail: david.hilton@phnt.swest.nhs.uk

3. Researcher/Data Co-ordinator

Mr Neil Bailey

*Division of Clinical Neurosciences
School of Medicine
University of Southampton
Mailpoint 806
South Academic Block
Southampton General Hospital
Tremona Road
Southampton
SO16 6YD*

Tel: 023 8079 4542
e-mail: N.E.Bailey@soton.ac.uk

4. Tissue Storage Centres

A list of all participating centres and relevant contact details are provided in *Appendix 1: Tissue Storage Centres*. Contact details for Designated Individuals and summary details of Human Tissue Authority Licensing arrangements for these sites are included in *Appendix 2: Human Tissue Authority Licensing*.

5. Funding

Medical Research Council
20 Park Crescent
London
W1B 1AL

Reference: G0701018
Grant ID: 82673

6. Sponsor

University of Southampton
University Road
Southampton
SO17 1BJ

n.b. Sponsorship application pending from University of Southampton.

7. Background

Neurological and psychiatric diseases represent an increasing social and economic burden for developed nations such as the United Kingdom^[1]. The progress towards effective therapy is being met with increasing frustration at the lack of translational success from animal and cell line models of neurological disease to the human disease itself^[2]. This has highlighted the need to study human brain tissue, derived from biopsies or from post mortem examinations, affected by the relevant disease processes. A limited number of specific neurological disorders, particularly chronic disorders such as Alzheimer's disease, Parkinson's disease and Multiple Sclerosis are well-catered for by high quality prospective brain banking facilities. However, many common and increasingly medically and economically important disorders in terms of mortality and morbidity, such as stroke, and most rare neurological disorders are not provided for in this way. There exists an opportunity to benefit from the extensive archival collections of human brain tissue held by neuropathology services around the UK and to exploit such holdings for high quality research to gain a better understanding of the aetiology and progression of a range of neurological diseases and disorders and to potentially allow therapeutic intervention strategies to be identified and developed. This research could, in the future, conceivably increase an individual's chances of survival, provide a better quality of care, contribute towards determining the evolving health needs of an ageing population and contribute towards the improvement of public health in the UK and beyond through improved therapeutic and medical practice.

Neuropathology, the identification, characterisation and diagnosis of neurological disease, based on the analysis of tissue, has existed as a defined speciality in the United Kingdom for several decades. Neuropathology services are located in approximately 30 NHS Neuroscience centres, each with a catchment population of 1 to 3 million people. After the macroscopic and histological analysis of human tissue derived from a post mortem examination has been completed it is archived according to guidelines published by the Royal College of Pathologists^[3]. This archive of pathologically verified residual tissue represents a potentially valuable resource for research purposes especially as it can be readily linked to relevant clinical data. However, to date there has been no systematic attempt to organise or to utilise this national resource for research purposes and this has been exacerbated in recent times by legal and ethical ambiguity surrounding the use and storage of human tissues. The passing of the Human Tissue Act 2004 (as applied to England, Wales and Northern Ireland), and the equivalent Human Tissue (Scotland) Act 2006, into law has removed this uncertainty and now defines archives held prior to the enactment of this legislation (*i.e.* before 1st September 2006) as 'Existing Holdings' which can be used, without explicit consent, for the purposes of ethically approved research provided that any material is anonymised to researchers^[4]. There is therefore a large amount of archived tissue that is of great potential value in increasing our understanding of neurological disease.

We have undertaken a limited pilot survey of five regional neuropathology services (Southampton, Plymouth, Oxford, Bristol and the Corsellis collection at Charing Cross Hospital, London) representing approximately 20% of the UK population. These preliminary data revealed 28,000 cases as being potentially available which extrapolates linearly to approximately 150,000 cases throughout the UK. These collections consisted predominantly of formalin-fixed paraffin embedded tissue which is ideal for the study of disease phenotypes in terms of morphological and protein expression analyses. Although arguably less powerful than the use of fresh tissue, this type of resource is also, through continuing technical advances, becoming increasingly amenable to the extraction of nuclear and mitochondrial DNA and RNA

for the study of the genetic influences on disease as well as the identification of infectious agents (e.g. viruses, bacteria and fungi) and the concomitant genetic study of such organisms. One major benefit of these collections is that they comprehensively cover the spectrum of neurological disorders, contain large numbers of common disorders, and provide useful numbers of rare disorders and non-diseased tissues suitable for control studies. These collections represent decades of work that would take a great deal of time and resources to accrue prospectively and this may indeed be impractical due to recent changes in autopsy practice^[5].

This proposal to create a national database of neuropathology tissue archives throughout the UK has the full support of the British Neuropathological Society (BNS) and the importance of such an initiative has been reiterated by bodies such as the Medical Research Council and the UK Clinical Research Collaboration which have identified a continuing need for the study of human brain tissue to further understand the basis and progression of neurological disease^[6].

8. Aims and Objectives

This initiative aims to establish the UK Brain Archive and Information Network (*BRAIN UK*) to maximise the potential to be gained from this valuable tissue resource for research into neurological diseases. The availability of high quality, well-characterised human brain tissue should form an essential and integral part of any systematic translational health research strategy for the UK. In contrast to established conventional brain banking facilities *BRAIN UK* will act as a 'virtual brain bank' with the tissue samples being retained in the departments of origin. This approach has been successfully used by the Confederation of Cancer Biobanks^[7] and the Cancer Research UK Bio-Specimen Biorepository^[8] and has a number of advantages over conventional brain banking facilities:

- A national archive with 'joint' ownership by all participating centres,
- Tissues from individuals are stored in the department of origin and are therefore readily available for diagnostic review if required,
- Not limited to diseases that can attract sufficient funding for dedicated brain banks,
- No major capital requirements and relatively low maintenance costs as existing facilities are utilised,
- Participating centres maintain full custodianship of tissue samples.

A linked anonymised electronic database will be created which will ultimately be made available, in a fully anonymised format, to the research community via the website of the British Neuropathological Society. The database, to be hosted by the University of Southampton, will include details of disease categories, together with the number of cases available, the tissue formats available and limited demographic data (sex and age at death). Access to archived tissue will be negotiated directly between the initiators of a research study and the local custodians of that tissue, once the relevant study has been approved. It is a primary aim of *BRAIN UK* to attempt to gain generic Ethical Approval for all research utilising tissue archived by participating centres (i.e. 'Existing Holdings') but, should this not be forthcoming, Ethical Approval should be obtained by the researcher in question as a prerequisite for access. It is intended that the technical and administrative costs incurred by the retrieval, processing and transportation of tissues will be met by the researcher's grant funding.

Letters of invitation to participate in this initiative have been sent to neuropathology centres and, at the time of writing, support has been received from 24 out of a total of 32 approached*.

* See Appendix 3: Participants
Ref: 09/H0504/68
UK Brain Archive and Information Network (*BRAIN UK*) Protocol v1.8
Date: 9 March 2009

9. Patient Eligibility

9.1 Inclusion Criteria

All patients who have had tissues removed and archived prior to 1st September 2006 as part of a post mortem examination (either Coronal/Fiscal Procurator or hospital/consented) in the UK (*i.e.* as part of an 'existing holding').

9.2 Exclusion Criteria

All patients who have had tissues removed and archived as part of a post mortem examination (either Coronal/Fiscal Procurator or hospital) in the UK where there is known evidence that consent has been refused (either by the patient during life or by a qualifying relative after death) for access to or disclosure from patient data or for the use of tissue for research purposes.

10. Consent, Privacy and Confidentiality

N.B. Expansion of this section is contained within the following policy and standard operating procedure document:

SOP 2: Data Confidentiality Policy

10.1 Consent

The use of human tissues that form part of an 'existing holding' is lawful for research purposes without consent if such research has gained a favourable opinion from a UK Research Ethics Committee and that any tissue is anonymised to any researchers (see Section 9.3 below). Consent for access to and disclosure from the computerised laboratory records of patients fulfilling the inclusion criteria with tissue(s) forming part of an 'existing holding' as defined by the Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006 will not be sought in the first instance for the following reasons:

1. Our pilot study indicated that there are approximately 150,000 potential cases throughout the UK that could be included as part of this initiative. To attempt to obtain consent from this cohort would be insupportable in terms of both time and expense.
2. Approaching relatives following bereavement could cause distress and harm especially if the nature of the bereavement related to a distressing condition or incident.
3. As many of the cases date from many years or decades ago it would be inappropriate to return to bereaved relatives so long after death.
4. There may be difficulty in tracing relatives or in contacting them many years after death due to factors such as migration and death.
5. The absolute requirement for consent would severely limit the size and scope of the database within available resources and diminish its potential benefits to the research community and the UK as a whole.
6. The use of linked anonymised data renders the probability that any individual could be identified by the recipient of such data to be extremely small. For practical purposes, this data may be considered as anonymous thus there is no concomitant requirement for consent^[9, 10] (see Section 10.2.3 below).

When pre-mortem wishes or preferences of the deceased are known and preclude the use of their tissues for research then such declarations will be respectfully honoured and such individuals will not be included on the database.

10.2 Section 251 National Health Service Act 2006

For the reasons cited above it is felt that obtaining rigid consent for access to and disclosure from the medical records of the deceased would be both impracticable and disproportionate. The implementation of measures to maintain patient anonymity and the common law duty of confidentiality (see Section 10 – Methods) and given that this initiative would potentially facilitate the undertaking of high quality research that could result in a direct patient benefit for individuals who develop neurological diseases and disorders in the future, it is felt that exemption from the requirement to obtain consent for the access to and disclosure from medical records under Section 251 of the National Health Service Act 2006 can be reasonably applied for in this instance.

10.3 Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006

The use of tissues that constitute an 'existing holding' as defined by the Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006 for the purposes of research is lawful without consent if the research has been ethically approved by a UK Research Ethics Committee and that such tissue is anonymised to the researchers. However, where the prior wishes of the deceased are known relating to the use of their tissue for research purposes it will be respected.

11. Methods

n.b. Expansions of this section are contained within the following policy and standard operating procedure documents:

SOP 1: Policy for Access to Archival Tissue Holdings of Participating Centres

SOP 3: Information Technology Security Policy

SOP 4: Data Extraction Policy

SOP 5: Policy for the Disclosure of Clinically Significant Information

11.1 Database Development, Management and Responsibilities

The database and all files (both electronic and paper) relating to it will be managed on a day-to-day basis by the designated Data Co-ordinator (Mr Neil Bailey). This individual will have core responsibility for undertaking procedures and arrangements for data collection, data anonymisation (where not already performed), data storage and data security. Data generated or accrued as part of this initiative will be accessible to only the Data Co-ordinator and the Chief Investigators until the creation of a secure fully anonymised database is complete.

11.2 Data Collection

11.2.1 Sources of data

Relevant data will be obtained from the computerised archives of each neuroscience centre participating in the *BRAIN UK* initiative. Where such records prove incomplete, reference will be made to paper records (e.g. pathology reports and autopsy reports) held by the same departments.

11.2.2 Types of data

Computerised laboratory records from participating centres will be accessed and data pertinent to the study will be accrued. These data will consist of:

- (i) Disease/diagnostic category,

- (ii) Systemised Nomenclature of Medicine Clinical Terms (SNOMED CT) number or equivalent,
- (iii) Number of cases of each disease category,
- (iv) Laboratory/Specimen/Post mortem number (dependent upon local practice and custom),
- (v) Specimen format (e.g. formalin-fixed paraffin-embedded tissue, formalin-fixed wet tissue, frozen tissue, cerebrospinal fluid, whole blood, plasma, serum, unstained slides, stained slides, tissue microarrays),
- (vi) Location,
- (vii) Custodian contact details (contact name, telephone number, fax number, e-mail address, full postal address),
- (viii) Matched clinicopathological data availability (e.g. pathology reports and autopsy reports),
- (ix) Simple demographic data (e.g. sex, age at death).

11.2.3 Linked Anonymised (Pseudonymised) Data

The inclusion of a specimen laboratory number (or equivalent) by definition will make the data stored on the database linked anonymised ('pseudonymised')^[10] in nature. From feedback we have received from those centres interested in participation there was a common feeling that the inclusion of laboratory numbers would make it more efficient for them to locate specific tissue(s) and medical data of interest for subsequent research activities. Although a laboratory number is potentially a personal identifier, the key relating to core personal details (e.g. patient name, date of birth, address, NHS number) will be held and maintained only by the participating host centre in question. No inference about the identity of an individual represented by a particular laboratory number can therefore be reasonably or easily deduced by the Data Co-ordinator or others. The data is therefore linked anonymised which is considered as anonymised for practical purposes when the key to patient identity is not held by the researcher as is the case here and that there is neither compromise to patient privacy nor a common law requirement to seek consent for their use under these circumstances^[9, 10].

11.3 Data Anonymisation

Ideally, and in the first instance, the removal of identifying information from accrued data will be performed within the originating organisation by a Healthcare Professional prior to it being disseminated as linked anonymised data to the Data Co-ordinator. However if, due to time or cost constraints, this could not be performed by the data custodians then data collection and anonymisation would be performed by the Data Co-ordinator. The Data Co-ordinator would take all measures to anonymise the data as soon as is practical resulting in linked anonymised data. As a single nominated individual would have this task this would present minimal risks of personal data being disclosed inappropriately and it would greatly reduce any scope for the infringement of the common law duty of confidentiality. This measure makes potentially sensitive personal data available to the least number of individuals possible and greatly reduces the scope for legal or ethical objection. The Data Co-ordinator would be bound by a duty of confidentiality as *per* the relevant policies produced by the University of Southampton and would be liable to the sanctions set out in such policies should inappropriate breaches of data security or confidentiality occur for whatever reason.

Shifting the burden of creating anonymised or linked anonymised data sets onto hospital pathology departments would be onerous and may create a reason for a centre not to become involved with this initiative. As comprehensive nationwide coverage is a primary goal of this initiative we consider that providing time resources to participating centres will make their

involvement more likely, and will provide a more representative and enduring data resource than would otherwise be the case.

11.4 Data Transfer

Linked anonymised data will be transferred from the site of origin to the central database by one of the following methods depending upon circumstance:

- (i) In electronic form using encrypted removable storage media (e.g. compact disc, USB drive or other electronic storage medium) via accredited secure courier services,
- (ii) Collected in person by the Data Co-ordinator and transported physically using encrypted removable storage media.

Given recent high profile security lapses in a range of UK organisational settings concerning the loss of sensitive data, measures maintaining the security of data during its transport or transfer from the originating site to the core database are considered to be of utmost importance. Therefore protocols for the safe and secure transportation or transfer of data will be developed in line with the recommendations of best practice contained within the NHS Information Security Management Code of Practice^[11]. The bulk extraction and transfer of data will also only occur once the specific authorisations of the Director responsible for the work area and the relevant Caldicott guardian have been received in line with the NHS Information Governance Framework^[12].

As there is enhanced scope for interception and unauthorised access using unencrypted or unisolated networks it is not considered good practice to transfer patient data, even in an anonymised format, via e-mail. **It is therefore important to stress that no data relating to the creation of the BRAIN UK database will be transferred by e-mail.**

11.5 Data Storage

During the creation of the database all electronic data will be stored on a dedicated stand-alone computer[¶] in the Data Co-ordinator's office. This computer will be isolated and will not be connected to Local Area Networks (LAN) and Wide Area Networks (WAN). The software to be used for the transfer of data will be either MS Excel 2003 v11.0 or MS Access 2003 v11.0 dependent upon the number of records present. The central database and those databases related to the researcher application process will be constructed using MS Access 2003 v11.0.

This computer will be found in the following location:

Room LD80C
Division of Clinical Neurosciences
School of Medicine
University of Southampton
South Academic Block, Mailpoint 806
Southampton General Hospital
Tremona Road
Southampton
SO16 6YD

Other University staff have access to this room during office hours (0900 – 1700) but the room is locked outside of these hours and at weekends. Access is via a keypad lock known only to the staff using the room as an office. All paper records generated will be filed and maintained within a locked cupboard in the above room and any electronic media (e.g. DVD/CDs or USB Flash drives) will be secured within a dedicated fire-proof safe.

[¶] See Appendix 4: Computer System Specification Summary
Ref: 09/H0504/68
UK Brain Archive and Information Network (BRAIN UK) Protocol v1.8
Date: 9 March 2009

11.6 Data Security

11.6.1 Password protection

All electronic data will be held on a single dedicated computer belonging to the University of Southampton. This computer is password protected by both BIOS and login passwords which are only known to the Data Co-ordinator. Account lockout will be activated if there are five failed password login attempts. There will be a policy of logging off from the computer if it is to be left unattended at any time and inactivity will activate a screen-saver login after 5 minutes. Security logs will be accessed on a weekly basis in an attempt to monitor any unauthorised access or attempts at access. For additional security the computer tower will be fastened securely to the workstation and a security filter fitted to the monitor to minimise inappropriate disclosure.

In addition, all computer files relating to the database will also be password protected which again will only be known to the Data Co-ordinator. However, for use in the event of unforeseen circumstances, copies of relevant passwords will be kept in a sealed envelope in a secure and locked location in the offices of the Chief Investigators.

Paper records that are generated as a consequence of this study will be filed in a locked cupboard in the Data Co-ordinator's office and electronic media will be stored in a dedicated fireproof safe. The keys to these facilities will be kept on the person of the Data Co-ordinator. Again, for use in unforeseen circumstances, duplicate keys will be kept in a secure location in the offices of the Chief Investigators.

11.6.2 Electronic file back-up

To ensure that the database remains patent regular backup of relevant electronic files will occur on a regular basis onto DVD/Compact discs. These media will be labelled and dated accordingly and kept securely in the Data Co-ordinator's office. As such storage media are prone to corruption after long-term storage, relevant files will also be backed-up onto a dedicated detachable hard drive which will be stored securely when not in use. All media used to back-up files will be encrypted. To ensure that computer files stored using these methods are not corrupted they will be accessed and tested on a regular basis to ensure patency.

11.6.3 Encryption

As the data to be employed on the database is linked anonymised and, as the key is to be held and maintained by the relevant participating centre, there is no easily achievable means whereby those holding such data (either as part of the research team or inappropriately outside of the research team) can reverse the process to identify any individual from the data they may have. In this situation, the data may be considered as anonymised^[9]. However, as a willingness to demonstrate the undertaking of best practice, all relevant files and storage media will utilise encryption to maintain the highest possible data security standards.

The encryption of electronic files and databases will be achieved using *TrueCrypt*[™] v6.1 (TrueCrypt Foundation, USA), an automatic, real-time and transparent encryption tool. This software will be used to create a mounted encrypted drive on the Data Co-ordinator's computer and to partition any electronic storage devices (such as a USB flash drive or removable hard drive) that will automatically encrypt or decrypt all data prior to it being saved or loaded from the partition drive.

To be used, the mounted drive will have to be activated each session using a 24 character password that will only be known to the Data Co-ordinator. Once the hosting computer has been shut down or requires pass word activation (e.g. screen-saver login), the mounted drive dismounts and would be invisible and inaccessible to any unauthorised individual rebooting that computer using the correct BIOS or login passwords. Data protected in this manner is block encrypted using a 256 bit Advanced Encryption Standard (AES-256) encryption algorithm and a 512 bit Secure Hash Algorithm (SHA-512) and files may only be accessed using the correct password.

All data transferred from the site of origination (either personally or via accredited courier services) to the central database will be encrypted according to NHS Approved Cryptographic Standards and transported securely following appropriate NHS guidelines.

As an additional security measure, and to demonstrate the willingness to adopt best practice, an encrypted external hard drive will be utilised to store data. This will prevent any unauthorised access to and modification of stored data and should maintain the security of any data as a consequence of loss or theft. The specifications of this device will be in line with NHS Approved Cryptographic Standards.

11.7 Research Uses of Database

Once completed, components of the *BRAIN UK* database will be made available to the UK research community in a fully anonymised format using the website of the British Neuropathological Society (<http://bns.org.uk/>) as a portal and will be hosted by the University of Southampton. Basic and superficial content will be available to browsers (e.g. disease category, number of specimens available UK wide, tissue format, sex, age range represented and number of participating centres holding relevant material) and functionality will be incorporated to enable browsers to undertake queries relating to sex and age if such variables are important to their intended research.

It is envisaged that the *BRAIN UK* database will be used as a means of facilitating high quality research by enabling researchers to determine which archive(s) contain those tissues of interest to their future and on-going investigations.

11.8 Applications From External Researchers

Once a researcher has identified relevant tissue pertinent to their research they are at liberty to make an application for access to tissue held by participating centres. This will be achieved via the use of a standard application form which will be submitted to *BRAIN UK* electronically with a signed paper copy being submitted by post. The application form will provide contact information, detail where the research is to be conducted and details of the types and quantities of tissue required. Each application will be supported by documentary evidence of a favourable ethical opinion (where applicable), sufficient funding, favourable peer-review, sponsorship and the study protocol (please refer to *SOP 1: Policy for Access to Tissue Archival Holdings of Participating Centres* for additional details).

Once all documentation has been received, each application will be considered against standard criteria and a decision relating to granting access to the *BRAIN UK* network of participating centres will be made by the *BRAIN UK* Director. This decision making process will be based upon whether the proposed research reaches a minimum threshold in terms of quality and design. Each application will also be disseminated to participating centres holding tissue of potential use for their opinion and it is important to note that each centre has the ultimate right to veto the use of their archive regardless of any decision made by *BRAIN UK*.

Once a favourable opinion has been received researchers will be put in contact with participating centres and vice versa. It is the responsibility of each participating centre and researcher to ensure that supply arrangements are in place to ensure the 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. In addition, it is the sole responsibility of the researcher to ensure that local R&D approvals have also been attained prior to undertaking any work. Costs incurred due to the retrieval, processing and transportation of tissue will be met by the investigator's grant fund.

The process of applying for access to the *BRAIN UK* network of participating centres will require that personal information of applicants will be held for a period of 5 years for the purposes of audit and to enable annual reports to be drafted. As a consequence, the Data Protection Act 1998^[12] will apply therefore *BRAIN UK* will adhere to the letter and spirit of this legislation to maintain data security and to ensure that all data is processed fairly and lawfully.

All policies and guidance relating to Data Protection published by the University of Southampton will be implemented and adhered to.

11.9 Ethical Approval

BRAIN UK will, in the first instance, be applying for generic ethical approval for the use of archived tissue at participating centres for the purposes of research. If granted, this would enable most research to be conducted without the requirement for individual researchers to obtain their own ethical approval and would greatly facilitate the process of neurological research. However, there may be occasions when *BRAIN UK* may feel it is appropriate for a particular study to receive additional scrutiny from a UK Research Ethics Committee. This would apply in particular to research requiring access to relatives of the deceased, broad access to clinical notes and medical histories and to research that has an above 'minimal' risk of generating data that would have clinical significance for the surviving relatives of a donor. Applying for such additional ethical approval would be the sole responsibility of the researcher and evidence of a favourable opinion would need to be submitted in support of an application.

11.10 Submission of Research Data

All researchers utilising tissue obtained from the *BRAIN UK* network of participating centres are obliged to submit the outcomes of their research to the *BRAIN UK* Director in the form of fully acknowledged papers and abstracts. In addition, research that yields data of a clinically significant nature, such as a modification or change to the diagnosis, should make such information available to both *BRAIN UK* and the NHS Trust from which the relevant sample originated so that a decision can be reached over whether to offer to disclose such data to the living relatives of that donor.

11.11 Offer to Disclose Clinically Significant Data

It will be the policy of *BRAIN UK* not to offer to disclose research data to the relatives of the deceased except in rare and exceptional circumstances. This decision has been based upon the following reasoning:

1. The tissue held is diagnostically verified therefore, for diseased tissues, there would be reduced scope to discover additional information of clinical pertinence. For instance, if an individual had died of Huntington's disease, it is probable that family members at risk would already have been identified and received appropriate counselling and testing. It is therefore assumed that the value of outcome has been determined and that subsequent life choices (e.g. reproductive decisions) would have been addressed.
2. The tissue archive collections are retrospective and, in some instances, extend back a number of decades. It would be inappropriate to return to individuals if many years had elapsed since the death of their relative; to do so may cause harm especially if the events surrounding such a death were traumatic.
3. The majority of neurological and psychiatric diseases and disorders remain incurable and there is limited scope in terms of effective curative therapy. Therefore the likelihood of an effective clinical outcome would remain low for most research particularly that relating to neurodegenerative disorders and dementias.
4. In terms of study context, there would be no existing relationship between the relatives of donors nor would it be likely that one would exist in the future. This would indicate, as a consequence, that to approach relatives would be inappropriate. However, if researchers were to pursue living relatives in terms of gaining additional clinical information as part of their study, this would require the approval of a UK Research Ethics Committee and this undertaking would be the sole responsibility of that researcher.

However, it is recognised that there may be very rare occasions when the question arises that it may be appropriate to offer to disclose clinically significant data. If so, the question will be considered by the *BRAIN UK* Committee which will seek appropriate advice and discuss the

possibility of disclosure with the relevant NHS Trust. In this event, the final decision to disclose will lie with the NHS Trust from which the relevant tissue was obtained for research purposes. The process and means of such a disclosure will follow the policies and guidelines of the particular NHS Trust in question.

12. Statistical Analysis

The data stored on the database will be utilised for crude and superficial data analysis to exemplify the content of the database (e.g. diagnostic categories represented, the number of specimens, types of holdings at each individual site). The representation of data will be through the use of simple diagrams e.g. pie charts, bar charts.

13. Ethical and Legal Considerations

As the data of interest is to be derived from the medical records (primarily the computerised laboratory records) of the deceased it is not covered by the principles and requirements of the Data Protection Act 1998 which relates only to the living^[13]. However, the medical records of the deceased are catered for by the Access to Medical Records Act 1990 but this legislation primarily relates to access to the medical records of the deceased by those who may have a claim arising from the patient's death and only applies to records created since 1st November 1991^[14]. More recently, there has been an indication that access may also be facilitated via the Freedom of Information Act 2000 and, at the time of writing, a review of this legal position was being undertaken jointly by the Ministry of Justice and the Department of Health but no guidelines have yet been published^[15]. However, the Bluck case^[16] would seem to indicate that disclosure may be exempted under Section 41 of the Freedom of Information Act 2000. In essence, access to the medical records of the deceased for research purposes represents a legal grey area exacerbated by a lack of case law on this subject^[17] and the lack of formal legal obligations to confidentiality that apply to the deceased^[18].

Although there is agreement upon the ethical basis for the maintenance of the privacy and the common law confidentiality of individuals and their relatives after death^[19], it is felt that the intended nature and scope of this initiative would make it insupportable in terms of available time and resources to undertake obtaining consent for access to and disclosure from the medical records of the deceased. To do so would also greatly diminish the power of the initiative and greatly restrict the scope, coverage and depth of the proposed database. Therefore, it is proposed that, as obtaining consent would be onerous and disproportionate, an approach will be made to the Patient Information Advisory Group (PIAG) to seek permission for disclosure under Section 251 of the National Health Service Act 2006.

In addition, there are ethical considerations pertaining to approaching the families of the deceased as this has the potential to cause harm or distress especially if the nature of the bereavement related to a distressing condition or incident. In addition, it would also be inappropriate to return to the bereaved family if a number of years have elapsed since the time of death as this may again have the potential to cause harm and revisit events that may have been adjusted to. With regards to the passage of time, it may also be difficult to locate family members to obtain consent due to migration or, indeed, death.

It is accepted that during the process of accessing the medical records and the anonymisation of any subsequent data that individuals may be privy to personal identifying information. It is intended that linked anonymisation will occur as soon as is practicable and that this process will either be undertaken by the original custodians of the data or by a single nominated individual within the *BRAIN UK* research team. This greatly minimises the access to such sensitive information and greatly reduces the scope for inappropriate dissemination of this information beyond the research team. In addition, there are contractual mechanisms and safeguards in place that would bring forward sanctions should there be a breach of confidentiality or an inappropriate disclosure of information.

We therefore feel, as safeguards are to be rigorously implemented concerning the security and confidentiality of any data accrued, that the proposal does not represent any significant or

unmanageable risks to the well-being or security of the families of the deceased. Also, given that the future research that could be facilitated by this initiative has the potential to be of benefit to such individuals, as well as society as a whole, we feel that this initiative will very much be in the best interests of the future health and well-being of the population of the United Kingdom and beyond. Disclosure of relevant patient information would therefore be in the public interest, be proportionate to need and would balance with the rights of the families of the individuals concerned whilst maintaining trust in what is a confidential service.

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