DEC BRAIN & BIOBANK FOR NEURODEGENERATIVE DEMENTIA AND CONCUSSION RESEARCH PROTOCOL

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Confidentially Statement

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disclosed must be informed that the information is privileged and confidential and it may not be further disclosed by them.

Investigator Agreement

DEC Brain & BioBank For Neurodegenerative Dementia And Concussion

I have read the protocol and agree that it contains all necessary details for carrying out this study.

I understand that all patient information in connection with this trial is considered confidential information. The information includes the clinical protocol, the Case Report Form, technical methodology and basic scientific data.

By my signature below, I hereby attest that I have read, understood and agree to abide by all conditions, instructions and restrictions contained in the above protocol.

Investigator:

_____	_____	_____
Name (print)	Signature	Date

Name and Address of Investigational Site:

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PROTOCOL SYNOPSIS

The investigators of this study aim to launch a BrainBank Biorepository in London, Ontario in collaboration with Scientists, Professors and Physicians (Neurologists & Neuropathologists) of London Health Sciences Centre, Western University and St. Joseph Health Care London. The biosamples of the bank will be located at Robarts Research Institute of Western University. Administrative offices will be located both at Parkwood and Robarts. Electronic database will be with the Lawson RedCap. The DEC Brain & BioBank for Neurodegenerative Dementia & Concussion is being launched to

facilitate scientific research by acting as a local and external resource for distributing well-characterized human biosamples (brain tissue, blood, cerebrospinal fluid) and clinical data among researchers in the community conducting research in the field of neurodegenerative brain disorders.

LIST OF ABBREVIATIONS

AD	Alzheimer's Disease
ALS	Amyotrophic Lateral Sclerosis
CJD	Creutzfeldt-Jakob Disease
CRF	Case Report Form
CTE	Chronic Traumatic Encephalopathy
FTD	Frontotemporal Dementia
GUID	Global Unique Identifier
HD	Huntington's Disease
ICF	Informed Consent Form
DECBB	DEC Brain & BioBank for Neurodegenerative Dementia and Concussion
LHSC	London Health Sciences Centre
MS	Multiple Sclerosis

MTA	Material Transfer Agreement
NDD	Neurodegenerative Disease
PD	Parkinson's Disease
PI	Principal Investigator
REDCap	Research Electronic Data Capture
SDM	Substitute Decision Maker
SJHC	St Joseph Health Care
UWO	Western University
WHO	World Health Organization

1. INTRODUCTION

1.1 BACKGROUND

Four years ago, a demographic milestone was reached across North America – the baby boomers began to become senior citizens. The proportion of the Canadian population over age 65 climbed from 11.6% in 1991 to 16% in 2016, and will be 23% in 2041[1]. As this demographic evolution occurs, the concerns and problems of elderly people will take center stage in Canada. Dementia is the single greatest cause of disability and debilitation in our senior population. Dementia is most commonly caused by large class of neurodegenerative disorders (NDDs) characterized by the progressive deterioration of thinking ability, memory, behavior, personality and movement as the brain becomes damaged[2]. It costs Canadians $15 billion a year to care for these population- a figure expected to grow ten-fold to nearly $153 billion by 2038[1].

A call to action has come internationally from the World Health Organization (WHO)[1] stressing that multidisciplinary research is essential and an appropriate balance must be struck between basic research on disease mechanisms, and applied research dealing with pharmacologic and non-pharmacologic approaches to the prevention, treatment, and care of those with dementia. There is an urgency to be able to identify those who will develop NDD before brain function is compromised, so that treatment may be enacted to maintain independence. Therapeutic approaches that are directed at single biological mechanisms or targets may be inadequate given the complexity of these multifaceted neurodegenerative disorders[3]. Successful treatments may vary depending on the stage of the disorder being treated, genetic predispositions, gender and mixed pathologies suggesting the need for a more personalized medicine.

When unraveling the complexities of neurological, neurodevelopmental, and neuropsychiatric disorders, there is no substitute for studying human brain tissue. Hence, brain donation is critically important. The more brain tissue available for research, the faster science can advance toward a better understanding of how to prevent, diagnose, treat, and cure disorders of the human brain.

Each donated brain is a precious resource, with the potential to provide tissue to hundreds of investigators. At the same time, each donated brain is ultimately non-renewable, and more are needed to keep pace with opportunities for new studies. Indeed, there are several disorders, including Parkinson's disease, traumatic brain injury, chronic traumatic encephalopathy, myalgic encephalopathy/chronic fatigue syndrome, autism, and down syndrome, for which there are vastly inadequate resources to meet the research demand. Access to brain tissue from healthy donors of all ages also remains a challenge, both for studies of normal brain structure and function and for use as controls in disease-focused research, where the ability to

compare tissues from people with and without a disease is critically important. Today, powerful new technologies allow researchers to examine molecular and micro-structural changes in psychiatric, neurodevelopmental, and neurodegenerative disorders that were previously undetectable, offering tremendous opportunities for research using human brain tissue.

Despite the presence of one of the Canada's strongest clinical and research programs in neuroscience and neurologic disorders, currently there is no brain bank or biorepository in the London, Ontario area for these conditions. There is no policy and place to store valuable human brain tissue post autopsy past the routine two year storage, leading to destruction and waste of valuable human brain tissue samples. The investigators of this study aim to launch a BrainBank biorepository in London Ontario in collaboration with scientists, professors and physicians of London Health Sciences Centre, Western University and St. Joseph Health Care London. DEC Brain & BioBank Neurodegenerative Dementia and Concussion (DECBB) is to coordinate brain donation, store tissues indefinitely and facilitate the distribution of high quality, well characterized human post-mortem brain tissue to qualified researchers locally and globally.

It is intended to foster innovative and collaborative research across Canada and internationally. This study will unite the tremendous resources of clinician researchers, basic scientists, social scientists, and allied professionals to explore the causes and improve the identification, management, treatment and prevention of NDD that lead to impairments in memory, cognition, and function. The following assessment platforms have been set up to simplify and smooth the process of brain donation for DECBB:

a. History - Demographics, medical, psychological, neurological, imaging

b. Biosamples and clinical impact of biomarkers

c. Genomics and epigenomics

d. Brain donation and neuropathology

1.2 JUSTIFICATIONS OF PLATFORMS

a. History (Demographics, medical, psychological, neurological, imaging, collection of GUID)

As with all medical conditions, a person's life experience and past and current overall health status can contribute greatly to understanding how NDDs emerge and express themselves within an individual. Data related to patients present and past clinical history will be acquired and stored in secured DECBB database.

Cognitive changes are core features of many neurodegenerative diseases. Specific patterns of cognitive strengths and weaknesses, quantified by neuropsychological testing, have been shown to help distinguish AD (Alzheimer's disease), FTD (Frontotemporal Dementia), Lewy Body Dementia (LBD), and other NDD from normal aging and each other. However, the full extent of these differences is still being researched as well as their earliest neuropsychological manifestations. We will be archiving data of any cognitive function test with the goal of furthering our understanding of these diseases and how they affect cognition.

Over the past decade, magnetic resonance imaging (MRI) and more recently positron emission tomography (PET) has taken a greater role in the management of patients with dementia[4]. For example, after diagnosis imaging can be used to increase the certainty that AD pathology underlies dementia. Prior to diagnosis, imaging can be used to establish the etiology of disease and may help predict progression to dementia.

Finally, in the pre-symptomatic phase, markers of amyloid accumulation and neurodegeneration can be used to establish pathophysiological changes in the brain[5]. The benefit of inclusion of imaging results will be in the form of the generation of new knowledge related to differential anatomical changes among the study cohorts.

b. <u>Biosamples and clinical impact of biomarkers</u>

Given the invasive nature of brain biopsy, currently definitive diagnosis of the NDD are made only with either genetic testing or in the majority of patients, post-mortem. Much current research is focused on identifying changes in molecules related to NDD that may be measured in blood[6] and CSF (cerebrospinal fluid)[7]. The importance of this is that it can help us to better understand the mechanisms and effects of neurodegeneration, as well as provide potential diagnostic markers, which may aid in earlier diagnosis of these diseases in the future.

Over the course of the past two decades, a number of biomarkers of neurodegenerative disease have been discovered that are highly specific for one type of NDD versus another[8]. The most informative biomarkers identified so far are CSF proteins amyloid beta and tau[9] which can confirm or disconfirm the presence of AD or FTD; structural MRI measures[10] which can confirm FTD, AD, and Vascular dementias; genetic profile[11-14] which can provide confirmation of vulnerability to cognitive decline; and fluid based biomarkers[15,16] which can distinguish PD (Parkinson's disease) and LBD from other types of NDDs[17]. Biomarker research will aid to develop novel biomarkers and assess if they can be of added benefit to current diagnostic system to be adopted for wider use in the medical community and whether policy should be developed to enable its wider use.

c. <u>Genomics and Epigenetics</u>

In the past 50 years, there has been considerable progress in delineating the etiologies of hereditary neurodegenerative disorders, including familial forms of AD, FTD, and LBD[18, 19]. The rare familial forms are single-gene disorders that result from rare mutations in a well-defined panel of genes for each disease; these can be detected using DNA sequencing methods. In addition, it is now appreciated that a substantial proportion of patients who present with these diseases clinically have a genetic susceptibility component that is cumulative of many common variants of small effect (single nucleotide polymorphisms [SNPs]), rare variants of large effect, as well as structural or copy number variants. The results of genome-wide association studies have allowed for genotyping of known SNPs to create a genetic risk score as the foundation of genetic susceptibility. A substantial proportion of the genetic susceptibility to these disorders remains unaccounted for, but may include epigenetic and mitochondrial effects.

d. Brain donation and neuropathology

In many NDD, a definitive diagnosis can only be made through brain tissue analysis, generally acquired at autopsy. Despite advances in diagnostic technologies, such as the advent of amyloid imaging, tissue pathology is still the “gold standard” for NDD diagnosis. It also represents an important tool to examine epigenetic and proteomic aspects of NDD [20-22]. As part of this study, we will be creating a voluntary Brain Donation Program tied to a London BioBank Biorepository in order to optimize the collection of brain samples and to standardize the handling and analysis of brain tissue across the region and integrate the tissue samples with the rich clinical history and information available. The benefit of this will be the creation of a local resource with feasible access to local researchers and will allow correlations between pathology and longitudinal clinical, neuropsychological and imaging data.

e. Global Unique Identifier (GUID) Collection

The BioBank will collect deidentified image, testing, demographic, medical history, family history, left over samples from other investigator initiated research studies at our site. As part of the process, participants having a National Institute on Aging (NIA) Global Unique Identifier (GUID) will be recorded in BioBank database. The GUID is a secure, random alphanumeric identifier. It can be used to match participants across studies and datasets without disclosing participants' Personal Identifying Information or Personal Health Information. The purpose of this GUID is to allow for the sharing of deidentified data and biospecimens between BrainBank and other research studies at our site such as GENFI.

1.3 RATIONALE

The prevalence of neurological, neuropsychiatric, and neurodevelopmental disorders continues to rise worldwide. These disorders can significantly impact the quality and length of life for affected people and their loved ones. The likelihood of being diagnosed with a neurological disorder continues to increase with age, and the lengthening lifespan means more people will likely suffer from these disorders. The need for research to further understand these disorders continues to be a priority. While substantial progress has been made in understanding these disorders, there are still many unanswered questions. The limited supply of donated tissues is a barrier to progress in understanding these diseases. Research using human brain tissue has the potential to identify new disease pathways and targets for therapeutic intervention. To be successful, such studies will require large numbers of high-quality, well-characterized brain samples and associated clinical data from donors.

London, Ontario serves as a centre of excellence for southwestern Ontario region for clinical and neuropathological evaluation of patients with neurodegenerative disorders and sport concussions. However, challenges that exist in the clinical diagnosis, identification of fundamental pathogenic mechanisms, unknown risk factors and lack of suitable treatments make post-mortem evaluations an important contributor to advancing these fields. Currently, infrastructure for the organization, processing, storage and linkage to other biosamples and clinical information is lacking. Furthermore, growing interest among established cognitive neurology clinics, sport concussion programs and acquired brain injury programs in London are presenting with patient populations with concussion but without existing neurodegeneration that would aid in global research efforts in identifying risk factors for the development of chronic traumatic encephalopathy (CTE) and other neurodegenerative disorders. The creation of the DECBB would facilitate research by providing invaluable brain tissue as well as other fluid biosamples from well characterized clinical patients to both local and external researchers, advancing science and ultimately, clinical care in this field. The addition of collecting blood and cerebrospinal fluid samples will considerably strengthen the usefulness of clinical data and post-mortem brain samples[23]. Over time as samples accrue, the DECBB will be a valuable resource that may facilitate recruitment of researchers, clinicians and neuropathologists in these fields to the Western University. As such, we propose the development and implementation of the DEC Brain & BioBank for Neurodegenerative Dementia and Concussion.

2. OBJECTIVES

2.1 GENERAL OBJECTIVES

The purpose of the DECBB is to facilitate scientific research by acting as a local and external resource for distributing well-characterized human biosamples (brain tissue, blood, cerebrospinal fluid) and clinical data among researchers in the community conducting research in the field of neurodegenerative brain disorders.

2.2 SPECIFIC GOALS

Currently, faculty and processes are in place for clinical and pathological assessments. The specific goals of the DECBB are to:

1. Establish the DECBB at Robarts Research Institute for the storage and archiving of frozen and fixed brain tissue, paraffin blocks, blood samples and cerebrospinal fluids (CSF).
2. Establish a local committee consisting of a Neuropathologists, Neurologists and community members to efficiently oversee maintenance and review requests for samples while facilitating local, national and external collaborations.
3. Distribute well-characterized, high-quality samples to local and external scientific researchers in the community.
4. Maintain local resource for fixed and frozen brain tissue and biosamples from persons with neurodegenerative brain disorders, and concussed but cognitively healthy participants obtained through clinical autopsy.
5. Transfer previously collected specimens from the aforementioned population to DECBB for storage providing investigators with access to tissue and clinical data for research.

6. Increase public awareness of the importance of the human brain donation and biosample collection for scientific research on brain diseases.

3. FACILITY

3.1 HOUSING TISSUE AND BIOSAMPLES

To accomplish its goals, the DECBB takes advantage of existing infrastructure of the Robarts Research Institute at Western University, London, ON. Robarts is a renounced neuroimaging facility in Ontario, Canada, equipped with the most advanced MRI and confocal microscopy tools for molecular pathology analysis. It has strong collaborative linkage to scientists and clinicians of Western's Robart's Research Institute, Lawson Health Research Institute, Brain and Mind Institute, London Health Sciences Centre, St Joseph Health Care Centre and is a crucial part of Western's BrainsCAN, fostering national and international collaborations in neuroscience.

The DEBB will be housed at Robarts Research Institute in London, Ontario and will act as a local and external resource for research in the field of neurodegenerative disorders and concussion. Biosample collection will be based at LHSC, University Hospital and at Parkwood Institute of SJHC London. Clinical neuropathological findings obtained from brain tissue will be incorporated in the BrainBank database (REDCap) with Lawson. Additional demographic, medical, neurological history and data will be acquired and stored in the specified database above. Proper security and de-identification will be in place to maintain confidentiality of participant's data.

The DECBB will not interfere with routine neuropathological or clinical activities at any affiliated or local site. It will utilize brain tissues obtained at affiliated sites, following the two year period of mandatory retention by LHSC, to provide ongoing storage and organization of these biosamples for future research.

3.2 ADMINISTRATIVE OFFICE AND ACTIVITIES

Administrative offices in related to the DECBB will be located at Parkwood Institute Main Building at the department of Cognitive Neurology as well as in Robarts Research Institute. Research coordinator will manage day-to-day operations of the Brain BioBank under the direction of Dr. Elizabeth Finger.

In accordance with its purpose and objectives, the DECBB will perform the following activities:

a. Ongoing recruitment of patients and healthy volunteer brain donors and provision of information regarding brain biobanking.

b. Study staff will conduct follow up assessments (phone/email) once a year to confirm donor's decision to participate in the study, update any change in clinical diagnosis, and update contact information for participant, study partner, primary care provider, care facility and designated mortuary, if applicable.

c. Obtaining and documenting informed consent from participant or substitute decision maker (informed consent given by a legal representative or next-of-kin on behalf of an individual unable to give informed consent).

d. Assist with coordination with participants' brain donation process (among next of kin, funeral home, autopsy, transportation, neuropathologist).

e. Documentation and storage of biosamples and data, and provide anonymity for all donor biosamples and related data into the study database.

f. Transfer brain and spinal cord tissue samples following clinical autopsy at LHSC at completion of two years routine storage, to the DECBB at Robarts Research Institute.

g. Maintenance of post-mortem tissue and biosample data to render suitable for research purposes.

h. Reviewing applications for distribution of research materials/biosamples.

i. Provide publication policies for researchers, and incorporate ongoing policies and procedures as deemed suitable by the directors of the founding committee, in compliance with the regulatory bodies for maintaining overall goals of DECBB.

j. Distributing biosample material and data (de-identified) to local and external entities on the basis of approved applications and providing researchers access to biosample materials and database.

3.3 DATABASE

All participant clinical data will be stored in a secure centralized password protected electronic REDCap Hospital database system of Lawson. Data will be entered and maintained in line with the principles of the Data Protection Act. Data stored are subject

to external audit by regulatory bodies to ensure compliance with the principles of good research governance.

When processing biosample materials and data, information stored is classified according to the degree of sensitivity. As such, identifying data, deemed highly sensitive, stored at the DECBB consists of:

a. Personal identifying data of living persons who are registered as a donor, including clinical diagnosis, medical and health records and additional data.

b. Identifying data of the next-of-kin, family member or legal guardians of the prospective or deceased donors.

c. A copy of identifiable patient records of the deceased donors, obtained from their physicians or health care providers.

d. Identifiable neuropathological biosample materials or data of the deceased donors.

e. Biosample materials with labels containing identifying information.

f. Any key for decoding pseudo-anonymized data that can be traced or identified as a living or deceased donor.

g. Any other biosample material and data of a confidential nature will be treated as such.

4. STUDY POPULATION

4.1 STUDY SAMPLE SIZE

Over the next 25 years we project to receive 6-20 brain donations/year at DECBB. This will be combined with the donated samples already stored at LHSC (~250 brain tissue samples). DECBB is expected to house up to 750 brain tissues and associated biosamples (from healthy, neurodegenerative disease donors) available to local and external research investigators.

4.2 INCLUSION AND EXCLUSION CRITERIA

Participants must meet each of the following criteria for enrolment into the study:

1. Written informed consent must be obtained and documented (from the participant or the substitute decision maker).
2. Geographic accessibility to the study site.
3. Living donors must have a study partner (next of kin or substitute decision maker) who can participate as required in the protocol to provide corroborative information.
4. Must be a patient of a physician affiliated with LHSC or SJHC, or referred in and accepted for clinical autopsy by an LHSC Neuropathologist.

Participants exhibiting any of the following conditions are to be excluded from the study:

1. The presence of malignant brain cancer, which oncologists are interested in keeping for tumor bank.

2. Living subject is not able to make decisions for him/herself due to cognitive deficits and does not have a study partner who can provide corroborative information.

3. Coroners cases retained by the coroner are exclusionary to the study. However cases which are released maybe accepted.

4. Pediatric population (under 18) are exclusionary to the study.

5. Infectious disease cases such as Prion or CJD, HIV, EBOLA etc any organism requiring beyond biosafety level 1 are exclusionary to the study.

4.3 DONOR COHORTS

The donor cohorts of the DECBB will include two populations, deceased and living.

4.3.1 DECEASED DONOR

This group is composed of deceased donors, on whose behalf the substitute decision maker donates the brain tissue to DECBB.

4.3.2 LIVING DONOR

This group is composed of alive individuals who gives consent to brain donation after death to DECBB. Among the living participants in the DECBB program there is further two sub groups:

I. Healthy (cognitively)

II. Neurodegenerative diseases

I. <u>Healthy</u>

Any healthy volunteer giving consent to brain donation after death to DECBB are incorporated in this group. This group also includes any participant who may have had concussions in the past but are cognitively healthy.

II. <u>Neurodegenerative disease</u>

Participants with any neurodegenerative disease giving consent while alive to take part in the study will be recruited to DECBB. Incompetent participants may provide consent through next-of-kin or substitute decision maker.

Participants who will not donate brain after death but who agree to donate left over biosamples (blood, CSF) obtained from standard of care or through other studies at Parkwood will be able to do so through signing a specific consent form assigned by DECBB.

In line with the purpose of the DECBB, any neurological disorder causing cognitive dysfunction can be included in the study. Brain and biosample will be collected, stored and distributed from the following (but not limited to) characterized brain disorders:

a. Neurodegenerative brain diseases (e.g. Frontotemporal Dementias and related disorders, Alzheimer's disease, vascular dementia, Parkinson's disease, Huntington's disease, Amyotrophic lateral sclerosis (ALS), Lewy Body Dementia, Adult Onset Leukodystrophy with Axonal Spheroids and Pigmented Glia (ALSP), Chronic Traumatic Encephalopathy and so forth).

b. Traumatic brain injury.

c. Autoimmune diseases leading to neurodegeneration (e.g. autoimmune encephalitis, Multiple sclerosis (MS).

5. STUDY PROCEDURE

5.1 RECRUITMENT

Brain banks require brain donors and, as such, reaching out to and enrolling interested candidates is an essential part of any bank's establishment[23]. We expect majority of our donors will be patients who will be approached face to face while they are at the hospital for care. Pamphlets will be provided for them to take home and discuss with family members on this process. DECBB will also setup a website to advertise and reach out to a larger pool of potential donors and ensure enrollment of a sufficiently-sized cohort to meet study needs. It may include advertising periodically through dedicated disease advocacy groups, national organizations, and in specialized newsletters tailored to the population of study to spread awareness about the brain donor program and promote recruitment. Recruitment of participants through telephone calls may also be used for potential donors who are current or past patients at Parkwood Institute.

5.2 SCREENING AND OBTAINING CONSENT

Once initial contact has been established, the next step is to properly screen interested donors. Although some candidates may be referred to brain banks by a knowledgeable health care professional, at other times potential donors with unconfirmed diagnoses

contact brain banks by their own initiative. Whatever the circumstances, it is up to the DECBB to verify these diagnoses to ensure the inclusion of only those cases that would benefit the research being done, and exclude those who should not contribute to the study. Screening methods may verify candidate viability by any combination of methods, including interviews and questionnaires, or soliciting medical records from providers.

The concept of informed consent has a prominent role in Brain Banking and as such, interactions between The DECBB and donors, their next-of-kin or representatives are deemed very important or the efficacy, progress and sustainability of the DECBB. The following information is made available to persons prior to signing an informed consent or authorization:

a. Information regarding the DECBB as an organization within LHSC, SJHC and Western University in the collection of human biological material.

b. Purposes for which biosamples and data are collected and stored.

c. Purpose of the registration at the DECBB.

d. Eligibility for registration and donation.

e. Possible restrictions that may be placed on the scope of informed consent or authorization.

f. The right to withdraw informed consent or authorization at any point in time and the consequences of withdrawal.

g. Eligibility and procedure of clinical autopsy in order to obtain biosample material for research as well as any risks associated.

h. Nature and amount of biosamples being taken and choices in that respect.

i. Nature and amount of personal/health/clinical data which will be collected and choices in that respect.

j. Where and how biosample materials and data will be stored and relevant security measures taken to preserve anonymity, as well as the potential risks for disclosure of personal information.

k. Who will have access to biosample material and data.

l. Conditions for which biosample material and data will be distributed.

m. How long biosample material and data will be stored and retained.

n. Arrangements for disposal of biosample material and choices in that respect.

o. Whether general results, incidental findings or future findings from prospective research will be disclosed to family of the donor.

Informed consent or authorization signed by the person in accordance with subsections a, b and c (above) should explicitly cover the following elements:

1. Consent to collect blood and optional CSF samples from consenting participants and retain samples for future research.

2. Consent to retain brain and spinal cord tissue samples obtained following routine clinical autopsy and to use them for research.

3. Permission to view medical/clinical records and to process data contained therein.

4. Statement that the prospective donor, representative or next-of-kin understands that informed consent or authorization can be withdrawn at any time and how this process should be completed.

5. When authorization on behalf of the deceased donor is signed by a representative or next-of-kin, a statement that to the knowledge of the representative or the next-of-kin no objection to post-mortem donation for research purposes or similar objection has been previously made by the deceased.

6. Consent to perform research which could generate genetic information/incidental findings.

A DECBB clinician will lead discussion about autopsy and brain donation with potential research participants and/or patients. Persons involved in the consent process are provided with the opportunity to communicate and have all questions answered. If research participants/patients wish to postpone their decision about donation, discussions are repeated at subsequent follow-up visits until a decision is made (consent or decline). If provisional consent is provided, the DECBB team works to ensure the participant and/or patient's wishes regarding brain donation are carried out and that family members, next-of-kin or a legal representative are aware of the person's wishes. Patients are assured that a decision to refuse autopsy and brain donation in no way affects their continuing clinical care. When required and appropriate, informed consent should be co-signed by the next-of-kin, a confidant or a witness of the donor. Standard consenting procedures for clinical autopsy at LHSC will be followed for all participants consenting to participate in the DECBB. Similarly, when required and

appropriate, post-mortem assent for participant in the DECBB of the next-of-kin is obtained.

When voluntary consent is granted, more detailed information regarding the procedures that follow at time of death, including telephone numbers to call and other guidelines are provided. Persons who consent to donation are strongly encouraged to share this information with their next-of-kin, a representative or personal clinician.

In the case biosample materials and subsequent data are to be used in a manner not anticipated in the original informed consent process, including for previously collected biosamples or data where the use may deviate from the original consent or where informed consent may not have been obtained at the time of collection, the use of such biosample material and data shall be:

1. Reviewed by a research ethics board/committee which will determine whether seeking re-consent or re-authorization is justified or necessary;

2. Biosample materials and data will be kept anonymized.

All consent and authorization forms will be attributed a unique and unidentifiable alphanumeric code and appropriately documented including any restrictions placed, or any instructions or special requirements imposed by the donor, next-of-kin or representative.

5.3 ENROLMENT

After signing consent, the participant will be enrolled in the study. Brain donations are obtained from individuals who register before death, and/or from next-of-kin who

authorize a postmortem donation. Eligibility for postmortem donation of brain and other tissues is determined by trained staff at the DECBB. Notification of a request for postmortem donation may come from surviving family members, treating physicians, hospital systems, donor services, organ and tissue banks, disease advocacy groups, specialized residential facilities, and/or collaborating medical examiners.

Trained individuals request and document consent for brain tissue donation from the deceased's next-of-kin or legally authorized representative. Individual requests for release of medical records, questionnaires, and/or interviews with individuals knowledgeable of the deceased are obtained according to IRB approved policies and procedures.

5.3.1 BLOOD AND DATA COLLECTION

The procedure will require about 30 minute and include a blood draw and filling out a data collection form with the coordinator. Approximately 50 mL of blood by standard venipuncture will be collected. Relevant current and past medical, mental, neurological, and sociodemographic information will be recorded in case report form (CRF). The data collected by coordinator from participant/next of kin includes the following (not limited to):

a. Age

b. Sex, Ethnicity

c. Education

d. Profession

e. Lifestyle (smoker vs nonsmoker, alcohol consumption, drug use, exercise etc)

f. Contact of participant and Study Partner (aka next of kin or substitute decision maker)

g. Current or past medical history of any infectious, metabolic, chronic or autoimmune disease

h. Current or past history of any neurological disorders or concussion

i. Family history of any neurological or genetic disease

j. Obtain permission to access participants existing medical records from physicians

5.3.2 LUMBAR PUNCTURE (OPTIONAL)

Should the participant give consent for obtaining CSF with lumbar puncture, another 1hour appointment would be made during the first visit and enrolment. Lumbar puncture will be done by a specialized physician at the hospital setting and will take approximately 60 minutes in total. Details of the procedures are as follows:

Patients must be lying in the lateral decubitus position on an examination or procedure bed, flexed, with the back horizontal and perpendicular to the bed throughout its entire length. It is important to ensure the patient is as flexed as possible, but shoulders should be perpendicular to bed, and knees and ankles should be symmetrically placed. Chorhexidine or iodine aqueous solution skin application will be applied around the site of puncture and continue in a concentric motion towards the iliac crest. Sterile drapes are placed to keep sterile conditions. CSF is collected from the

vertebral interspace L3-L4 as indicated by a line joining the tips of the iliac crests or L4-L5. Lidocaine 1% is administered subcutaneously. A lumbar puncture needed is inserted in the L3-4 or L4-5 interspace. Up to 10 mL of CSF will be collected. All tubes and polypropylene containers will be labeled with correct ID for the subject. CSF samples will be aliquoted into 0.5 ml polypropylene containers and then stored in a -80 fridge until they can be transported via cryoshipper to the DECBB at Robarts for permanent storage.

After the lumbar puncture is completed, participant will remain in the clinic for about 20 minutes for monitoring (so the visit will take 1 hour altogether). Participant will also be given something to eat and drink before leaving. Participant will be advised not to do any strenuous physical activity for the next 48 hours such as weight or other heavy lifting or straining. Study staff will call the participant day following the lumbar puncture to discuss how participant is feeling.

5.4 STUDY FOLLOW UP

After the initial enrolment visit, study coordinator will follow up with phone calls periodically to confirm participants' decision to stay with the study; to verify contact information of the donor and their study partner, their primary care provider, residential or care facility staff and designated mortuary, if applicable. Participant will be provided a wallet-size enrollment card to sign and carry with them containing the DECBB contact info. They will receive information about how to contact site staff at the time of death. This will help the post-mortem arrangements to be carried out smoothly.

5.5 AUTOPSY

Autopsies will be carried out at London Health Sciences Centre, University Hospital by licensed and registered neuropathologists of the Western University. A research coordinator in affiliation with the DECBB is designated to process all DECBB consent forms, provide information as requested by donors and their families or representatives, and monitors the necessity to update any information. At the time of death, the coordinator facilitates arrangements to ensure the completion of the autopsy. Valid clinical autopsy consent form from LHSC will be completed by the next of kin and processed by the Department of Pathology clinical team according to current standard operating procedures. The coordinator verifies that the neuropathologist or autopsy technician has the necessary measures to send the required biosample tissue to the DECBB.

The donor's next-of-kin or representative will notify Parkwood Institute staff as soon as possible following the time of death. A London Health Sciences Centre Autopsy Authorization (clinical consent) form must be completed for the subsequent autopsy to follow. The DECBB coordinator can help to facilitate (after the participant's death):

a. Contact next-of-kin or legal representative to clarify autopsy procedure. Obtain information about the funeral home they plan to use.

b. Contact the pathologists' assistant who will be assisting the post-mortem examination and brain removal. The pathologists' assistant will contact the neuropathologist who will be performing the autopsy.

c. Once neuropathologist and location have been identified, contact donor's funeral home and make arrangements for transportation of the body to and from University Hospital Autopsy Suite. Also obtain preliminary costs for these procedures.

d. Ensure clinical neuropathological examination of donated brain and biosample tissues is completed (generally takes 6-12 months). Results of the clinical neuropathological autopsy are made available to the patient's physicians and family as per standard operating procedures by the Department of Pathology, LHSC. When available, the neuropathologic diagnosis and molecular subtyping information will be entered into the DECBB database.

e. Two years following autopsy and routine clinical storage of brain and spinal cord tissue, the Department of Pathology and Laboratory Medicine of LHSC will coordinate the transfer of fixed and frozen brain and spinal cord tissues from the LHSC clinical storage unit to the DECBB at Robarts Research Institute.

5.5.1 TISSUE PROCESSING

Brain and spinal cord tissue specimens are excised, weighed, photographed and bisected at the time of autopsy in the morgue. One hemisphere is fixed in formalin, dissected in tissue blocks, paraffin embedded, sectioned and stained for neuropathological examination and diagnosis. The other hemisphere is preserved for distribution.

Samples of brain and other tissues are processed for the widest use by the neuroscientific community. In addition to the preparations described above, end-users may require brain and tissue samples at particular stages of neurological disease, and/or may require specific brain, brainstem or spinal cord loci, which require careful microdissection. The lab technicians use standardized anatomic procedures guided by

established landmarks to ensure regional samplings of the brains are processed with precision and uniformity.

Specimens will be generally available as,

a. Formalin fixed paraffin-embedded glass slide mounted sections suitable for routine histology, immunohistochemistry and molecular genetic analysis.

b. Frozen tissue samples from frontal, temporal and cerebellum will be retained at -80^{0}C.

c. Alternatively, the unfixed brain will be bisected during autopsy and one half will be frozen and kept at -80^{0}C. This will be done only with special request.

Extra formalin-fixed paraffin-embedded (FFPE) blocks can be sampled from wet formalin-fixed brain tissue after the autopsy report has been completed and these blocks will be identified by a given DECBB number and not the previous LHSC autopsy number. The sampling can be done by DECBB personnel under the supervision of the neuropathologist.

5.5.2 NEUROPATHOLOGY

All brain specimens donated to the DECBB are assessed and reviewed by board-certified neuropathologists. A standard assessment is performed to document possible neuropathologies and to establish diagnosis of disease condition. Gross inspection of the brain includes assessment of regional atrophy and inspection of macroscopic lesions and blood vessels for vascular disease. Brains are photographed in multiple planes to document the gross features and macroscopic abnormalities of each donation.

A two stage logical algorithm-based strategy is followed for microscopic neuropathological assessment of all donor brain specimens[24, 25]. In the first step, the clinical presentation of each donor is reviewed along with a screening assessment of the brain. Following gross examination of the brain, watershed territories (Brodmann areas 4,3,1,2), basal ganglia and cerebellum are sampled, H&E (hematoxylin-eosin) stained and microscopically evaluated. For all donors ≥65 years of age the screening protocol is followed by the full neuropathological assessment described below. For donors below age 65, clinical assessments are reviewed for any indication of brain-related disorders with known physical impact on the brain. If clinical evidence for such disorders is identified, the brain receives a full disease-appropriate neuropathological assessment. If the review of the clinical history does not endorse the presence of discernable neuropathology, then, the neuropathological screening protocol is implemented to rule out unsuspected pathology. If this screen reveals any indication of neuropathology, then a full evaluation is performed using stains for the indicated neuropathology. If there is no clinical history of a brain disorder with identifiable histopathology or systemic disease with neuropathological consequences, and the neuropathology screen confirms the absence of any pathologic process, then the neuropathological assessment is determined to be complete.

Neuropathological assessment of brains from aged persons (≥65) or donors with a clinical diagnosis of neurologic disease are examined with immunohistochemistry performed in multiple brain regions, including: superior and middle frontal gyrus, orbital cortex, watershed territories (Brodmann areas 4,3,1,2), basal ganglia with basal forebrain, amygdala, hippocampus (rostral and caudal levels with adjacent amygdala, parahippocampal and inferior temporal cortex), superior temporal gyrus, parietal cortex (angular gyrus), calcarine cortex, hypothalamus with mammillary bodies, thalamus, substantia nigra, midbrain at the level of the SN, pons including LC, medulla including

DMV, cerebellar vermis, lateral cerebellar hemisphere and cervical spinal cord. In addition to these standardized brain regions, additional sampling is performed based on clinical history or neuropathology review and findings where applicable.

Histochemistry and immunohistochemistry can include, but is not limited to: H&E, modified Bielschowski, thioflavin S, anti-beta-amyloid, alpha synuclein, phosphorylated tau and TDP-43. Cerebrovascular pathology is assessed using an adaptation of the protocols described by the Vinters group[26]. The vessels of the circle of Willis are photographed and evaluated semiquantitatively. The extent of arteriosclerosis is also assessed semiquantitatively. Congophilic angiopathy is rated using the criteria developed by Vonsattel group[27]. Ischemic lesions are tabulated and mapped as: cystic infarcts; lacunar infarcts; and microinfarcts. The hippocampus is evaluated separately for sclerosis.

Following the completion of the neuropathology evaluation, a report is generated indicating major neuropathological findings. This report is available to researchers and to the donor's family / next-of-kin, by request.

5.5.3 SEROLOGY AND TOXICOLOGY

Postmortem brain and tissue donations are not tested for HIV-1/2, Hepatitis B surface antigen (HBsAg), Hepatitis B surface antibody (anti-HBs) and Hepatitis C. Information on infectious disease is obtained from participants medical records. Irrespective of serology findings, all users are advised to exercise universal precaution (CDC-1987) for blood borne pathogens when handling human tissue biospecimens.

Postmortem analysis of nicotine, alcohol, illicit drugs and pharmaceuticals are not performed routinely on the majority of cases in the DECBB biorepository unless there is a clear indication (coroner's case, no anatomical cause of death found etc). If toxicology analysis is performed the results will be available for brain and tissue samples from the DECBB.

5.6 WITHDRAWAL

Participation in the brain donation study is completely voluntary. A decision not to participate will not result in any penalty or loss of benefits or standard of care to which the participant may be entitled to. Participant may wish to withdraw from the study at any point. In this case the collected fluid sample will be destroyed as per hospital procedures and all data information removed from BrainBank database. Should participant's relatives or substitute decision maker wish to withdraw the sample from the bank, it can also be accomplished in the same manner stated above. A study staff will help with such process. However, any sample or data that has already been shared with other researchers (before the withdrawal request is made) can no longer be retrieved. Requests to withdraw previously given consent or authorization will be promptly responded by the DECBB, taking care to:

a. Identify the person along with his or her request.

b. Explain the consequences of withdrawal and choices in that respect.

c. Explain the way biosample materials and data will be disposed of and choices in that respect.

d. Inform the person who in the past, has given consent or authorization and is now submitting a request for withdrawal that any biosample material and data which already have been used for research cannot be recalled and that a record of previously given consent or authorization will be retained.

e. A unique reference number of the withdrawn consent or authorization including any particular or special instructions placed by the donor, next-of-kin or a representative, will be retained in a withdrawal registration.

6. ADVERSE EVENT AND SERIOUS ADVERSE EVENT REPORTING

6.1 DEFINITIONS

I. Adverse Event (AE)

An adverse event (AE) is any untoward medical occurrence in a subject that may present itself during the conduct of a research study and which may or may not have a causal relationship with the study procedures. An AE can therefore be any unfavorable or unintended sign (e.g., including an abnormal laboratory finding), symptom, or disease temporally associated with a study procedure. An AE may be a new illness, worsening of a sign or symptom of a condition, or an effect from a study procedure.

I. Serious Adverse Event (SAE)

A serious adverse event (SAE) is any untoward medical occurrence that:

a. Results in death.

b. Is life-threatening, i.e., the subject was at immediate risk of death at the time of the event; it does not include any event which hypothetically might have caused death if it had occurred in a more severe form.
c. Requires inpatient hospitalization or prolongation of existing hospitalization. Hospitalizations and/or surgical procedures that are scheduled to occur during the study period, for an illness or disease that existed before subject enrolment in the study, will not be considered AEs provided the pre-existing condition did not deteriorate (e.g., surgery performed earlier than the planned date).
d. Results in persistent or significant disability or incapacity.

Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate. In other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above. These should also usually be considered serious.

6.2 ATTRIBUTION

The relationship of the AE to study procedure will be assessed by the investigator to be not related, unlikely, possible, probable or definite, as follows:

a. Not related: No relationship between the AE and the study procedure, judged clearly and incontrovertibly due to extraneous causes such as concomitant medication(s) or the subject's clinical state.

b. Unlikely: The AE is more likely due to an alternative explanation such as concomitant medication(s), concomitant disease(s) and/or the time relationship suggests that a causal relationship is unlikely.
c. Possible: The AE might be due to a study procedure. An alternative explanation such as concomitant medication(s), concomitant disease(s) is inconclusive. The time relationship is reasonable therefore the causal relationship cannot be excluded.
d. Probable: The AE might be due to a study procedure. An alternative explanation such as concomitant medication(s), concomitant disease(s) is less likely. The time relationship is suggestive, i.e. it is confirmed by de-challenge.
e. Definite: The AE cannot be reasonably explained by an alternative explanation such as concomitant medication(s), concomitant disease(s). The time relationship is very suggestive, i.e. it is confirmed by de-challenge and re-challenge.

For the purposes of safety analyses, all SAEs classified with a relationship to a study procedure of possible, probable or definite will be considered study-related events.

6.3 PROCEDURES FOR AE AND SAE REPORTING AND MONITORING

All AEs experienced by the subject following signing of informed consent and any study procedure must be reported and recorded in the CRF. For both serious and non-serious AEs, the investigator must determine both the intensity of the event and the relationship of the event to study procedures.

All SAEs will be recorded in the CRF. The initial SAE report should include at a minimum: subject number, a narrative description of the event, and an assessment by the investigator of the intensity of the event and relationship of the event to study procedure. The initial SAE report should be complete as soon as possible. A complete follow-up SAE report must be submitted to DECBB when the information, not available at the time of the initial report, becomes available. The DECBB sponsor may request SAE follow-up information.

All AEs and SAEs should be monitored to determine the outcome or until the investigator consider it medically justifiable to terminate follow-up.

7. ETHICAL CONSIDERATIONS

The current study will be conducted in compliance with the protocol, International Conference on Harmonization Good Clinical Practice (ICH-GCP) and the applicable regulatory requirements. All staff including all delegated researchers will have undertaken GCP training. Copies of GCP training certificates will be held centrally.

7.1 INSTITUTIONAL REVIEW BOARD

All relevant documents for this study will be submitted to an appropriate Institutional Review Board (IRB) or Independent Ethics Committee (IEC) for review. A signed and dated letter documenting IRB/IEC approval must be obtained prior to entering subjects at the site. The IRB/IEC must be notified of all subsequent protocol amendments.

7.2 INFORMED CONSENT

Prior to any study procedures, it is the responsibility of the investigator to fully inform the subject, substitute decision maker or legally acceptable representative, of all pertinent aspects of the study. Each subject, substitute decision maker or a legally authorized representative must give written consent prior to the subject's participation in the study. The method of obtaining and documenting the informed consent and the contents of the consent must comply with ICH-GCP and all applicable regulatory requirement(s).

7.3 CONFIDENTIALITY OF SUBJECT RECORDS

The REDCap database system of Lawson will house the data. It will store data that has been processed to remove any direct identifiers of an individual study participant. Study subjects will be assigned a unique coded study identification number, which will be used to store their data in DECBB.

The investigator will grant monitor(s) and auditor(s) from regulatory health authorities' access to the subject's original medical records for verification of the data gathered and to audit the data collection process. The participant's confidentiality will be maintained and the participant's information will only be made publicly available to the extent permitted by the applicable laws and regulations.

In cases where participant identification is required, the recruiting site study investigator for the participant will be informed and be given access to only the minimum identifying information required to link the participant to the incidental finding and move it towards a resolution.

Data from this study that has had identifying information removed to the extent possible may be shared with researchers and organizations that are not part of this study. This open approach is being used by researchers internationally to better understand disease. Access to data by outside researchers or organizations will require a detailed plan for the use of the data, and approval from a research ethics board, as described in DECBB's Data Sharing Policy. These researchers or organizations will be required to enter into an agreement with DECBB that clearly states the safeguards that will be in place to protect the data, and the purposes for which this data may be collected, used, stored and disclosed.

DECBB may take some of the data and combine it with data from many other people, and make it available to enhance the public's awareness of research. Tools will be used to remove identifying information from these combined data sets, making the risk of identifying the participant negligible.

8. ADMINISTRATIVE REQUIREMENTS

8.1 PROTOCOL AMENDMENTS

The Sponsor may modify the protocol at any time during the life of the protocol. Protocol amendments will require IRB/IEC approval prior to implementation except when changes to the protocol are required to eliminate immediate hazards to the study subjects. The Sponsor and IRB/IEC must be notified immediately after such changes have occurred.

8.2 PREMATURE TERMINATION OF THE STUDY

If the investigator or Sponsor discovers sufficient reasonable cause for the premature termination of the study, the terminating party will provide written notification documenting the reason for study termination. The appropriate regulatory agencies and IRB/IEC must be notified.

8.3 ACCESS TO SOURCE DATA AND DOCUMENTS

The investigator will permit study related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

8.4 RETENTION OF STUDY DOCUMENTS

The investigator must retain all study records for 25 years according to applicable regulatory requirements. If the investigator retires, relocates or withdraws from the responsibility of keeping the study records, custody must be transferred to a person willing to accept the responsibility. The regulatory bodies must be notified in writing if a custodial change occurs.

8.5 BIOLOGICAL SAMPLE AND DATA ACCESS POLICY

Biological samples will be stored at the Robarts Research Institute, Western University, London. The samples and clinical de-identified data will be available for investigators who wish to perform research. Access to these samples and data will be regulated by the Biological Sample & Data Access Committee which is made up of members from

DECBB. Requests for access will be assessed for feasibility, scientific rigor, and alignment with the consent of the participants. Samples will be shared with researchers both within Canada and Internationally. The full Biological Sample Access policy document is under development and will be made available upon its finalization.

8.5.1 DISTRIBUTION OF BRAIN BIOSPECIMENS AND TISSUES

All requests for brain and tissue specimens are to be placed through the application to the DECBB, available on the website (under development). Following review and approval by DECBB, staff coordinator will fill the request based on specimen availability. If questions arise, the requestor is contacted to clarify and confirm study design. Requestor's must follow the Tissue Request Instructions including the Tissue Request Guidelines and Tissue Request Standards when submitting a request.

DECBB end users are required to provide an account number with a shipping carrier to cover the costs of shipping the approved specimens. Shipping usually will occur between 4-6 weeks following approval; however, large requests may take longer to process. If the shipment is intended for a foreign country, the researcher is responsible for obtaining the required documents for entry of biohazardous material. Material and data transfer agreements required for such transfers will be completed between the Department of Pathology, LHSC and the requesting institution.

Points to be aware of or note in the request include,

a. Clarification of amount of tissue or number of sections needed.

b. Clarification of number of cases and unaffected controls requested.

c. Method validation in postmortem human brain.

d. Sample size required for pilot vs full study.

e. Lack of availability of specific requested cases and the need for substitution

By accepting tissue from the DECBB, the researcher attests in the signed DMTA (data and material transfer agreement) to acknowledge in all publications and presentations DECBB as the source of tissue (e.g., "Human tissue was received from the DECBB at the Western University and the Lawson Health Research Institute"). Recipients are required to submit a summary progress report no later than 1 year after receipt of the tissues.

It is essential that individuals exercise universal precautions when handling samples from postmortem human subjects. All samples should be treated as if they are infected with bloodborne pathogens, even if evidence suggests otherwise (e.g., a subject is reported to be HIV negative). The materials received are experimental in nature and may have hazardous properties.

The provider makes no representations and extends no warranties of any kind, either expressed or implied. The recipient will use the material with all due skill and care and with dignity, sensitivity and respect. Unless prohibited by law, the recipient assumes all liability for claims for damages against it by third parties which may arise from the use, storage or disposal of the material except that, to the extent permitted by law, the provider will be liable to the recipient when the damage is caused by the gross negligence of willful misconduct of the provider.

8.6 PUBLICATION POLICY

Prior to submission for publication or presentation of any data or results obtained in this study, written permission from the DECBB Publication Committee is required. Draft manuscripts, abstracts and presentations should be submitted to the Committee for review and approval. Authorship of publications resulting from this study should accurately reflect the academic contribution of individuals to the design and implementation of the study, analysis of the data and preparation of the manuscript. No researcher shall include identifiable personal health information in any publication or presentation. All publications that arise from the use of data contributed by the participating institution will give acknowledgement, attribution, or co-authorship as appropriate in accordance with the International Committee of Medication Journal Editors (ICMJE) standards and any rules established by the data access committee of DECBB.

8.7 FINANCING

The DECBB will be funded through:

a. Financial contributions by donors through LHSC Foundation.

b. Grants obtained by local PIs involved in the DECBB.

8.8 CESSATION OF BRAINBANK OR SUCCESSION PROCESS

The local committee of the DECBB, in consultation with donor representatives and other stakeholders, may make decisions regarding the cessation of all or part of the Brain Banking activities. Plans to terminate all activities and a call for succession, including any eligibility criteria will be announced upon such a decision. The local committee in

conformity with the above mentioned, will consider all eligible organizations for the succession of all materials and biosamples, and all Brain Banking activities, including the donor program.

Any such succession shall be formalized by a transfer agreement signed by both parties, upon which, all biosample material and data stored at the DECBB, including all donor registrations and material transfer agreements shall be transferred to the successor which is subject to the acceptance of provisions of these regulations or similar provisions for the governance and management of the succeeded resources.

In the case that no suitable successor is available or deemed fit for succession, all material and data stored at the DECBB will be irreversibly destroyed. All donors or next-of-kin will receive written and/or verbal notification of the cessation of all Brainbank activities. Upon either succession or termination as described previously, the DECBB may cease to exist.

9. CONFIDENTIALITY

All confidential information, verbal and written, provided to the investigator by the Sponsor will be kept in strict confidence, and restricted to the study personnel involved in conducting the study, except if the information is required by the IRB/IEC or similar committees.

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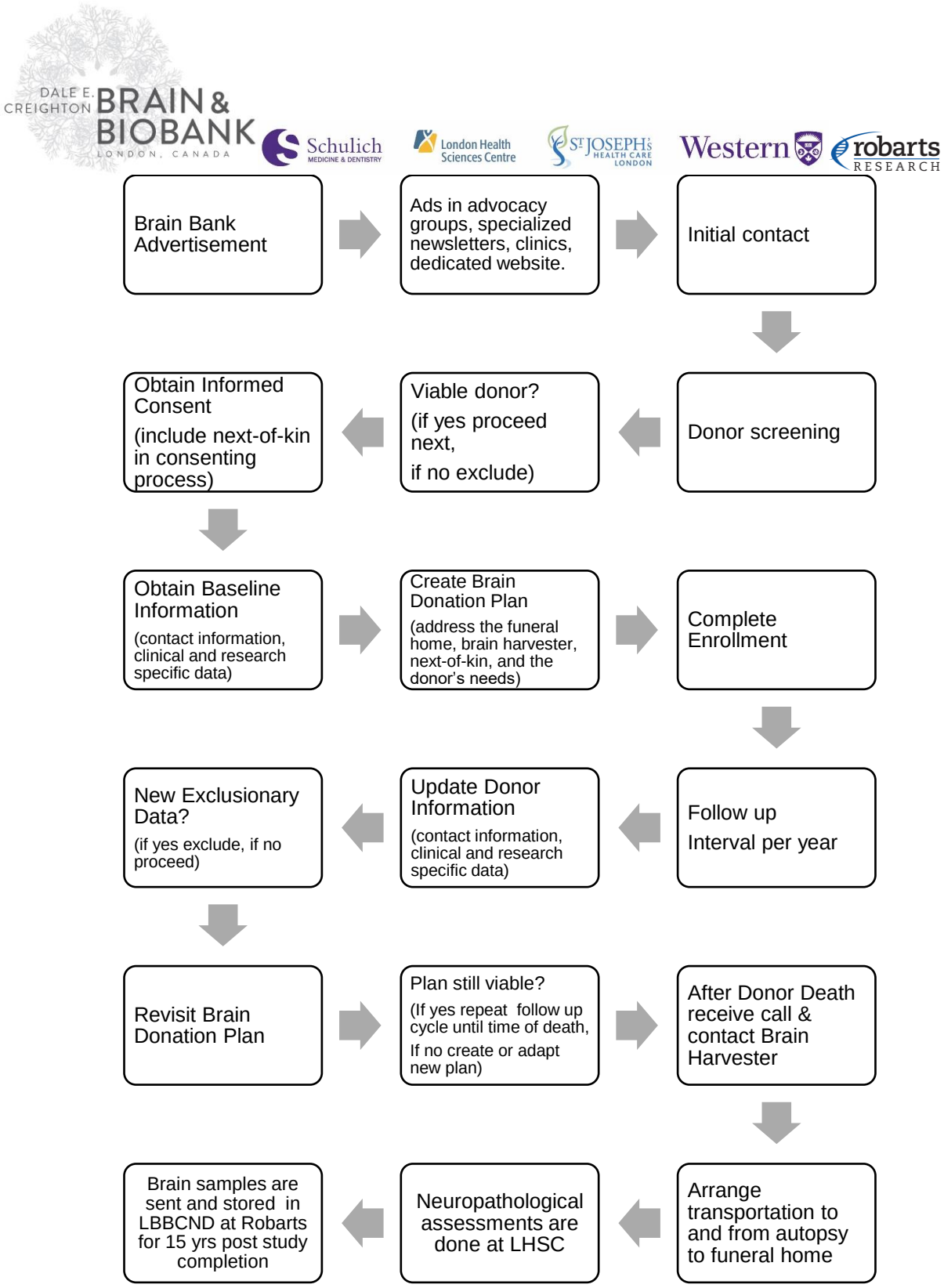
Appendix A: Wallet sized card, front and back, given to living participant when consent signed.

The undersigned has registered intent for BRAIN DONATION upon death, for purpose of research, with the DEC Brain & BioBank for Neurodegenerative Dementia & Concussion (DECBB), *(Parkwood Institute, SJHC London)* Name_____ Date_____ Signature_____	AT TIME OF DEATH: Contact the DEC Brain & BioBank for Neurodegenerative Dementia & Concussion (519-646-6032): Monday-Friday, 8 a.m - 5 p.m. (226-926-3760): Weekends or evenings

Appendix B: Flowchart of brain donation process.


Brain Bank Advertisement
Ads in advocacy groups, specialized newsletters, clinics, dedicated website.
Initial contact
Donor screening
Viable donor?
(if yes proceed next,
if no exclude)
Obtain Informed Consent
(include next-of-kin in consenting process)
Obtain Baseline Information
(contact information, clinical and research specific data)
Create Brain Donation Plan
(address the funeral home, brain harvester, next-of-kin, and the donor's needs)
Complete Enrollment
Follow up
Interval per year
Update Donor Information
(contact information, clinical and research specific data)
New Exclusionary Data?
(if yes exclude, if no proceed)
Revisit Brain Donation Plan
Plan still viable?
(If yes repeat follow up cycle until time of death,
If no create or adapt new plan)
After Donor Death receive call & contact Brain Harvester
Arrange transportation to and from autopsy to funeral home
Neuropathological assessments are done at LHSC
Brain samples are sent and stored in LBBCND at Robarts for 15 yrs post study completion

Appendix C: Flowchart of sample collection and storage process.