THE UNIVERSITY OF WESTERN ONTARIO
BIOLOGICAL AGENTS REGISTRY FORM
Approved Biohazards Subcommittee: October 14, 2010
Biosafety Website: www.uwo.ca/humanresources/biosafety/

This form must be completed by each Principal Investigator holding a grant administered by the University of Western Ontario (UWO) or in charge of a laboratory/facility where the use of Level 1, 2 or 3 biological agents is described in the laboratory or animal work proposed. The form must also be completed if any work is proposed involving animals carrying zoonotic agents infectious to humans or involving plants, fungi, or insects that require Public Health Agency of Canada (PHAC) or Canadian Food Inspection Agency (CFIA) permits.

This form must be updated at least every 3 years or when there are changes to the biological agents being used.

Containment Levels will be established in accordance with Laboratory Biosafety Guidelines, 3rd edition, 2004, Public Health Agency of Canada (PHAC) or Containment Standards for Veterinary Facilities, 1st edition 1996, Canadian Food Inspection Agency (CFIA).

Completed forms are to be returned to Occupational Health and Safety, (OHS), (Support Services Building, Room 4190) for distribution to the Biohazards Subcommittee. For questions regarding this form, please contact the Biosafety Officer at extension 81135 or biosafety@uwo.ca. If there are changes to the information on this form (excluding grant title and funding agencies), contact Occupational Health and Safety for a modification form. See website: www.uwo.ca/humanresources/biosafety

PRINCIPAL INVESTIGATOR	Dr Terry Peters
DEPARTMENT	Medical Imaging and Medical Biophysics
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EMERGENCY PHONE NUMBER(S)	519.438.3379, 519.902.3379 (cell)
EMAIL	tpeters@robarts.ca

Location of experimental work to be carried out: Building(s): Robarts Research Institute Rooms: 0270, 0270A

*For work being performed at Institutions affiliated with the University of Western Ontario, the Safety Officer for the Institution where experiments will take place must sign the form prior to its being sent to the University of Western Ontario Biosafety Officer (See Section 15.0, Approvals).

FUNDING AGENCY/AGENCIES: CIHR
GRANT TITLE(S): Image Guided Surgery for Epilepsy MOP-89844

List all personnel working under Principal Investigators supervision in this location:

Name	UWO E-mail Address	Date of Biosafety Training
Cathie Crukley	ccrukley@imaging.robarts.ca	February 9, 2011
Maged Goubran	mgoubran@imaging.robarts.ca	TBD
Elvis Chen	chene@imaging.robarts.ca	TBD
Diego Cantor	dcantor@imaging.robarts.ca	TBD

Please include a one page research summary or teaching protocol.

Epilepsy is a chronic neurological disorder that results in repeated spontaneous seizures affecting up to 1% of the general population, placing a large economic and social burden on society. According to an Ontario Health Survey in 1990, the quality of life, family function and social support are worse among the epileptic population compared to other chronically ill subjects, resulting in a significantly higher burden of illness on society than other chronic illnesses. More than 30 percent of the patients with epilepsy have inadequate control of seizures with drug therapy, and are considered to have epilepsy refractory to medical therapy. A standard ATL usually involves resection of the amygdala, a portion of the hippocampus, and anterior 4.0 to 4.5 cm of the lateral temporal cortex. Selective amygdala-hippocampactemy has shown similar efficacy in surgical outcome of TLE without demonstrating a significant improvement in cognitive outcome. These results lead us to believe that further improvement in refining the extent of surgical resection is required to improve the outcome. This is particularly relevant in patients without any apparent anatomical lesions in their imaging studies, or those with dual pathology, i.e. mesial temporal sclerosis (the commonest pathology in these patients) plus an extra-temporal pathology such as focal cortical dysplasia or tumour.

The objective of this proposal is to enhance current techniques to improve these outcome figures by integrating cutting-edge MRI methods, such as relaxation mapping, and diffusion tensor imaging (DTI), within a single visualization and planning environment, to provide both enhanced localization of epileptic foci, as well as to suggest optimal resection strategies. It also aims to correlate histological findings from excised tissue with high-resolution in-vivo and ex-vivo imaging of the affected brain tissue. This approach is intended ultimately to eliminate the need for invasive and traumatic procedures, such as the Wada test (that anesthetizes a hemisphere) and the application of cortical and deep brain EEG electrodes commonly employed to lateralize epileptogenic activity and identify seizure foci. Although the Wada test can be used to determine language lateralization and determine language function, it cannot detail the specific cortical regions involved in various language or memory tasks nor specify the degree of plasticity-dependent intrahemispheric shifts that have been described in epilepsy. This project will combine the results of multiple MR testing protocols implemented on a state-of-the-art 3T MRI, with tools developed in our laboratory during the previous funding cycles of this grant, and a unique digital histology environment that will allow objective validation of tissue signatures obtained from MR imaging.

The overall goal of this proposal will be the development of an environment that can serve as both a multi-spectral image analysis and diagnosis platform, and provide direct input for intra-operative surgical planning and guidance.

The specific objectives to achieve this goal are:

Create normal multi-spectral population database reflecting relaxation parameters T1 and T2.
Create a similar multi-spectral population database reflecting diffusion parameters MD and FA.
Compare patient data with this database to identify abnormal regions in patient MRI data.
Create 3D digital histology volumes of excised temporal lobe samples that can be registered to in-vivo and ex-vivo MR images of the same structures as a means of understanding the significance of the abnormal multi-spectral data.

This represents the first time that in-vivo and ex-vivo image data imaging will be directly correlated with high resolution digital histology volumes.

2.3 Please indicate the type of established cells that will be grown in culture in:

Cell Type	Is this cell type used in your work?	Specific cell line(s)*	Containment Level of each cell line	Supplier / Source of cell line(s)
Human	O Yes O No			
Rodent	O Yes O No			
Non-human primate	O Yes O No			
Other (specify)	O Yes O No			

*Please attach a Material Safety Data Sheet or equivalent from the supplier. (For more information, see www.atcc.org)

2.4 For above named cell types(s) indicate PHAC or CFIA containment level required O 1 O 2 O 2+ O 3

3.0 Use of Human Source Materials

3.1 Does your work involve the use of human source materials? X YES O NO
If no, please proceed to Section 4.0

3.2 Indicate in the table below the Human Source Material to be used.

Human Source Material	**Source/Supplier /Company Name**	**Is Human Source Material Infected With An Infectious Agent? YES/UNKNOWN**	**Name of Infectious Agent (If applicable)**	**PHAC or CFIA Containment Level (Select one)**
Human Blood (whole) or other Body Fluid	N/A	O Yes O Unknown		O 1 O 2 O 2+ O 3
Human Blood (fraction) or other Body Fluid	N/A	O Yes O Unknown		O 1 O 2 O 2+ O 3
Human Organs or Tissues (unpreserved)	University Hospital	O Yes X Unknown		O 1 X 2 O 2+ O 3
Human Organs or Tissues (preserved)	N/A	Not Applicable		Not Applicable

4.0 Genetically Modified Organisms and Cell lines

4.1 Will genetic modifications be made to the microorganisms, biological agents, or cells described in Sections 1.0 and 2.0? O YES X NO If no, please proceed to Section 5.0

4.2 Will genetic modification(s) involving plasmids be done? O YES, complete table below O NO

Bacteria Used for Cloning *	Plasmid(s) **	Source of Plasmid	Gene Transfected	Describe the change that results from transformation or tranfection

* Please attach a Material Data Sheet or equivalent if available.
** Please attach a plasmid map.

7.0 Use of Animal species with Zoonotic Hazards

7.1 Will any animals with zoonotic hazards or their organs, tissues, lavages or other body fluids including blood be used (see list below)? O YES X No If no, please proceed to section 8.0

7.2 Will live animals be used? O YES O No

7.3 If yes, please specify the animal(s) used:

- Pound source dogs O YES O NO
- Pound source cats O YES O NO
- Cattle, sheep or goats O YES, please specify species _____ O NO
- Non-human primates O YES, please specify species _____ O NO
- Wild caught animals O YES, please specify species & colony # _____ O NO
- Birds O YES, please specify species _____ O NO
- Others (wild or domestic) O YES, please specify _____ O NO

7.4 If no live animals are used, please specify the source of the specimens:

_____

8.0 Biological Toxins

8.1 Will toxins of biological origin be used? O YES X NO If no, please proceed to Section 9.0

8.2 If YES, please name the toxin(s)_____
Please attach information, such as a Material Safety Data Sheet, for the toxin(s) used.

8.3 What is the LD_{50} (specify species) of the toxin_____

8.4 How much of the toxin is handled at one time*? _____

8.5 How much of the toxin is stored*? _____

8.6 Will any biological toxins be used in live animals? O YES, Please provide details:_____ O NO

*For information on biosecurity requirements, please see:
http://www.uwo.ca/humanresources/docandform/docs/healthandsafety/biosafety/Biosecurity_Requirements.pdf

9.0 Insects

9.1 Do you use insects? O YES X NO If no, please proceed to Section 10.0

9.2 If YES, please give the name of the species. _____

9.3 What is the origin of the insect? _____

9.4 What is the life stage of the insect? _____

9.5 What is your intention? O Initiate and maintain colony, give location: _____
O "One-time" use, give location: _____

9.6 Please describe the risk (if any) of escape and how this will be mitigated:

_____

_____

13.0 Containment Levels

13.1 For the work described in sections 1.0 to 9.0, please indicate the highest HC or CFIA Containment Level required. O 1 X 2 O 2+ O 3

13.2 Has the facility been certified by OHS for this level of containment?
O YES, date of most recent biosafety inspection: _____
X NO, please certify
O NOT REQUIRED for Level 1 containment

13.3 Please indicate permit number (not applicable for first time applicants): _____

14.0 Procedures to be Followed

14.1 Please describe additional risk reduction measures will be taken beyond containment level 1, 2, 2+ or 3 measures, that are unique to this agent.
_____N/A_____
_____
_____

14.2 Please outline what will be done if there is an exposure to the biological agents listed, such as a needlestick injury or an accidental splash:

In case of needle puncture, express wound to bleed, wash with soap and water for 5 minutes. Contact Staff/Faculty Health.

14.3 As the Principal Investigator, I will ensure that this project will follow the Western Biosafety Guidelines and Procedures Manual for Containment Level 1 & 2 Laboratories (and the Level 3 Facilities Manual for Level 3 projects). I will ensure that UWO faculty, staff and students working in my laboratory have an up-to-date Hazard Communication Form, found at http://www.wph.uwo.ca/

SIGNATURE _____ Date: 27/01/11

15.0 Approvals

1) UWO Biohazards Subcommittee: SIGNATURE: _____
Date: _____

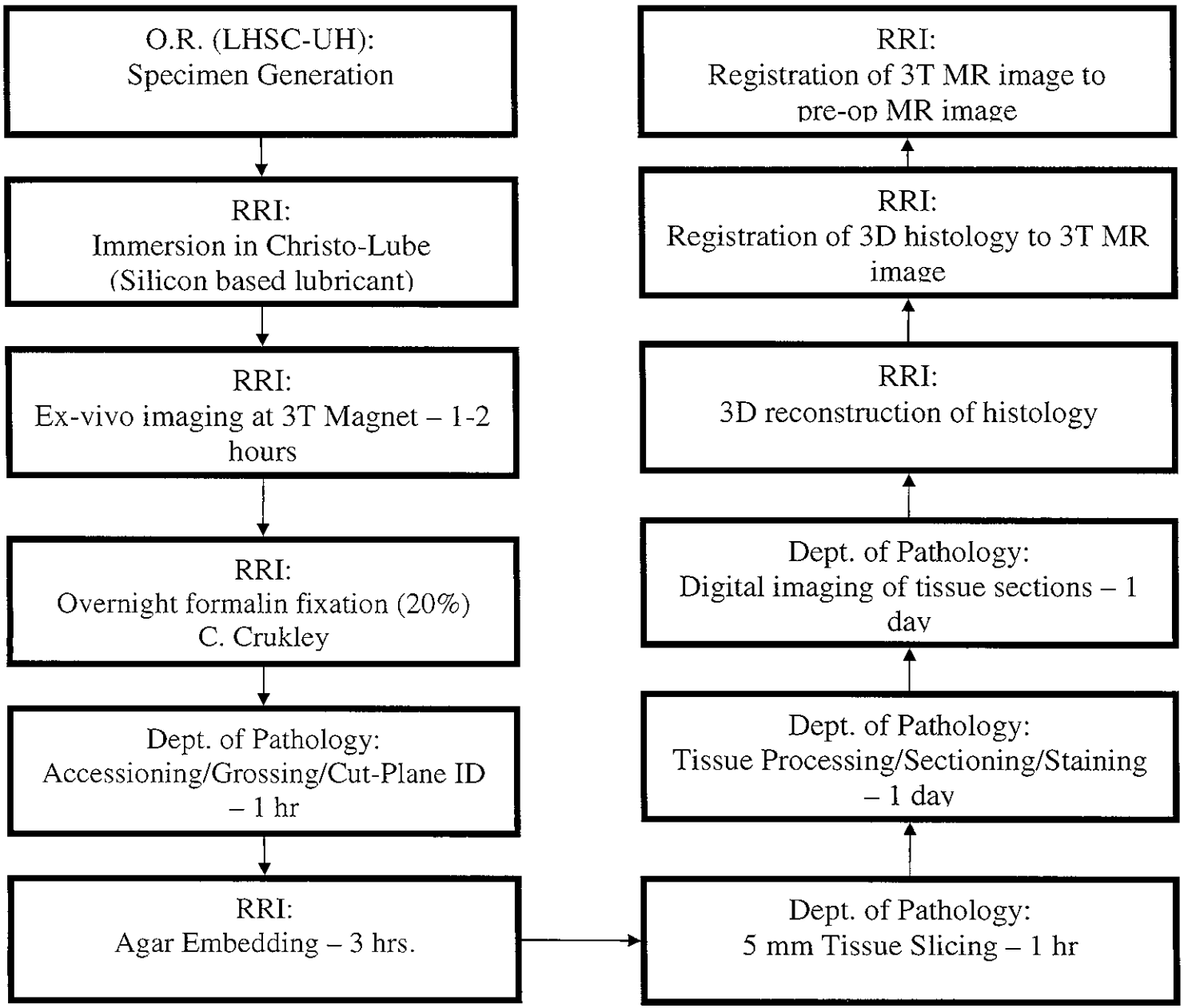
2) Safety Officer for the University of Western Ontario
SIGNATURE:_____
Date:_____

3) Safety Officer for Institution where experiments will take place (if not UWO):
SIGNATURE: Ronald Mesbarth
Date: January 31, 2011

Approval Number: _____ Expiry Date (3 years from Approval): _____

Special Conditions of Approval:

Protocol: Pathoanatomic Validation of resected temporal lobe epilepsy tissue by Multispectral MR imaging



Important notes:

A log book will be used to document all tissue sign in/out. The time and date of each transaction will be signed by a department of pathology staff member, and by the receiving/returning researcher.

All tissue sign outs and returns will be only be performed by Cathie Crukley (pathology research technologist) or Maged Goubran (graduate student).

Each signed out specimen will retain constant supervision by the receiving researcher. All specimen processing will be performed in a dedicated pathology lab at RRI under the supervision of a skilled pathology technologist (Cathie Crukley).

TITLE: Preparation of Temporal Lobe Epilepsy Study Specimens for MRI	
ID:IPL-443-02	File Name: EPI-EX TA#443
Eff: 01/01/11 Rev:	Authorized: Dr. T. Peters

Preparation of Temporal Lobe Epilepsy Study Specimens for MRI

PURPOSE:

To prepare unfixed human temporal lobe specimens for MR imaging.

EQUIPMENT:

- Acrylic splash guard
- Leak proof specimen transport container
- Forceps
- Labeled specimen container of an appropriate size for the designated MRI coil
- Christo-lube (Lubrication Technology Inc./cat# MCG 1046)
- Gauze
- Parafilm
- Self adhesive bandage (3M/ cat#1582)
- Virox5 disinfectant (Virox Technologies Inc., cat#53808)
- Plastic bag

SAFETY:

Universal precautions must be observed and all processes are to be carried out in a Biosafety Level 2 facility.

For safe handling of human biological material refer to UWO Biosafety Guidelines and Procedures Manual[1]. Wear appropriate PPE (lab coat, gloves, goggles, etc.)[2]. Refer to Material Safety Data Sheets (MSDS) for safe handling, disposal and storage of [illegible] substances.

Use BSC
← MRI area?
PN
Feb. 01, 2011

PROCEDURE:

1. Working within the acrylic splash guard, wrap t
within the diameter of the designated specimer
2. Place the wrapped specimen in the container a
space as possible.
3. Place the cap on the container and disinfect the
4. Seal the container with Parafilm and self adhes
5. Place the specimen in a leak proof specimen tra
suite.

REFERENCES:

1. http://www.uwo.ca/humanresources/facultystaff/h_and_s/biosafety/biosafety_policies.htm
2. Laboratory Biosafety Guidelines. 3rd edition. Ottawa: Public Health Agency of Canada, 2004

TITLE: Receipt and Transport of Temporal Lobe Epilepsy Study Specimens	
ID:IPL-443-01	File Name: EPI-EX TA#443
Eff: 01/01/11 Rev:	Authorized: Dr. T. Peters

Receipt and Transport of Temporal Lobe Epilepsy Study Specimens

PURPOSE:

To safely document and transport unfixed human temporal lobe specimens from the LHSC Operating Rooms to Robarts Research Institute.

EQUIPMENT:

- Leak proof specimen transport container
- Ice or ice pack
- Plastic specimen bag

SAFETY:

Universal precautions must be observed.

For safe handling of human biological material refer to UWO Biosafety Guidelines and Procedures Manual[1]. Wear appropriate PPE (lab coat, gloves, goggles, etc.)[2].

PROCEDURE:

1. Check in at the front desk of the Operating Room Suite and have the clerk inform the staff in the patient's OR that you have arrived to collect the study specimen.
2. Confirm that the sample will be brought out in a specimen container without fixative and that a completed Pathology requisition will be included.
3. Receive the specimen (confirming identity) and record the transaction in the study log with signatures to provide specimen tracking.
4. Insert the specimen and requisition into a marsupial type plastic bag and place onto the ice in the transport container, seal the container.
5. Transport the specimen to RRI, rm# 0270A for MRI preparation.

NOTE:

The patient's specimen and requisition are to be transported and stored in a secure manner to maintain confidentiality, away from unauthorized persons. The only identifier applied to subsequent containers used within RRI will be the patient's study number.

REFERENCES:

1. http://www.uwo.ca/humanresources/facultystaff/h_and_s/biosafety/biosafety_policies.htm
2. Laboratory Biosafety Guidelines. 3rd edition. Ottawa: Public Health Agency of Canada, 2004