The University *of* Western Ontario
BIOLOGICAL AGENTS REGISTRY FORM
Approved Biohazards Subcommittee: October 14, 2011
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).

Electronically completed forms are to be submitted to Occupational Health and Safety, (OHS), (Support Services Building, Room 4190 or to jstanle2@uwo.ca) 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.

Please ensure that all questions are fully and clearly answered. Failure to do so will lead to the form being returned, which will cause delays in your approval and frustration for you and your colleagues on the Committee.

If you are re-submitting this form as requested by the Biohazards Subcommittee, please make modifications to the form in bold print, highlighted in yellow. Please re-submit forms electronically.

PRINCIPAL INVESTIGATOR:	**Dr. Leonard Luyt**
DEPARTMENT:	**London Regional Cancer Program**
ADDRESS:	**790 Commissioners Rd. E.**
PHONE NUMBER:	**519-685-8600 x53302**
EMERGENCY PHONE NUMBER(S):	**519-282-1665, 519-434-9287**
EMAIL:	**lluyt@uwo.ca**

Location of experimental work to be carried out :

Building : **Victoria Hospital** Room(s): **A3-125**
Building : _____ Room(s): _____
Building : _____ Room(s): _____

***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: **NSERC, Prostate Cancer Canada**

GRANT TITLE(S): **Metal-organic compounds as scaffolds for the exploration of biologically relevant chemical space. (NSERC)**
Validation of the Ghrelin Receptor as a Target for the Molecular Imaging of Prostate Cancer. (PCC)

UNDERGRADUATE COURSE NAME(IF APPLICABLE): _____

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

Name	UWO E-mail Address	Date of Biosafety Training
Leonard Luyt	**lluyt@uwo.ca**	**December 5, 2012**
André St. Amant	**astaman@alumni.uwo.ca**	**August 27, 2012**
Ashley Esarik	**aesarik@uwo.ca**	**July 19, 2012**

Emily Simpson	esimpso8@uwo.ca	August 22, 2012
Lihai Yu	lihai_yu@hotmail.com	May 28, 2012
Milan Fowkes	mfowkes@uwo.ca	August 22, 2012
Carlie Charlton	ccharlt3@uwo.ca	August 28, 2012
Neha Sharma	nsharm63@uwo.ca	August 24, 2012

Please explain how the biological agents are used in your project and how they are stored and disposed of. The BARF without this description will not be reviewed.

The biological agents are being used in studies of receptor binding affinity.

The biological agents are stored labelled in a dedicated biological fridge.

The biological agents are destroyed using bleach and disposed of following our facility's waste disposal procedure.

Please include a ONE page research summary or teaching protocol in lay terms.
Forms with summaries more than one page will not be reviewed.

Organometallic OBOC libraries. While many protein targets have known endogenous ligands that can be used as a starting point for imaging agent discovery, the wealth of targets being discovered without known ligands requires a combinatorial approach to ligand discovery. The challenge is to efficiently discover imaging agents for these orphan targets. We and others have utilized one-bead one-compound (OBOC) combinatorial libraries as a chemical approach for de novo ligand discovery. The classical approach to using OBOC for imaging agent discovery is to use a split-mix peptide library, discover ligands with target affinity and then modify the structure to incorporate an imaging component, such as a radiometal-complex. This modification will affect the ligand's affinity for the protein target and an entirely new structure-activity process may be required. By including the radiometal-complex within the OBOC library there is an ability to screen organometallic libraries, which results in the discovery of imaging agents as lead candidates. Our preliminary work evaluated four Re(CO)3 complexes placed at the N-terminus of an octapeptide OBOC library. The isotopic signature of Re-185/187 assists in providing N-terminal fragment (b ion) identity upon MALDI-TOF/TOF sequencing. Furthermore, by placing an organometallic complex at the N-terminus, the metal complex is likely to be associated with ligand-target interaction and possibly be required for affinity. Thus, when created as a Tc-99m radiotracer, any non-chelated starting material will have lower target affinity and the effective specific activity would be improved. The ability to include organometallic species at the N-terminus and randomly within an OBOC library will be explored. The organometallic libraries will be screened using "beads on a bead" or cell incubation techniques, with automated flow sorting, allowing for the discovery of an imaging agent and subsequent validation using small animal imaging. OBOC libraries containing Ga-69/71 will also be pursued and offers a similar isotopic signature advantage for MALDI sequencing.

Plant viruses as a nanoplatform for molecular imaging. There are a number of significant advantages to using plant viruses as a nanoparticle platform, as they are: non-pathogenic, biodegradable, of consistent size and shape and are readily modified through standard bioorganic techniques . It is our goal to explore radiolabelled VNPs (viral nanoparticles) for the purpose of discovering a nanoparticle platform capable of targeted PET imaging. Two monodisperse VNP platforms will be explored, the spherical CPMV (30 nm diameter) and the rod shaped tobacco mosaic virus (TMV, 18 x 300 nm). In order to develop a robust strategy for multi-functionalization, azide-alkyne cycloaddition will be used, allowing for selective addition of peptides, metal chelators, fluorescent dyes, and/or pharmacokinetic modifiers such as PEG chains, hyaluronic acid or other polysaccharides. In the instance of the VNP containing a metal chelator such as DOTA or NOTA, radiolabelling with Ga-68 will generate a PET agent. Alternatively, if a F-18 labelled compound is desired due to its longer half-life, a prosthetic group approach will be employed whereby a F-18 containing small molecule will first be prepared and then added to the VNP. It is our desire to optimize the subsequent modifications and characterize the nanoparticles by MALDI, TEM, SDS-PAGE and micro-flow cytometry.

A binding study will consist of a radioisotope labelled compound being incubated with cells. Afterwards the cells are destroyed using bleach, held until the radioisotopes are decayed, then disposed of following our facility's waste disposal procedure.

1.0 Microorganisms

1.1 Does your work involve the use of biological agents? ☒ YES ☐ NO
(non-pathogenic and pathogenic biological agents including but not limited to bacteria and other microorganisms, viruses, prions, parasites or pathogens of plant or animal origin)? If no, please proceed to Section 2.0

Do you use microorganisms that require a permit from the CFIA? ☐ YES ☒ NO
If YES, please give the name of the species ____________________
What is the origin of the microorganism(s)? ____________________

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

Please attach the CFIA permit.

Please describe any CFIA permit conditions:

1.2 Please complete the table below:

Full Scientific Name of Biological Agent(s)* (Be specific)	Is it known to be a human pathogen? YES/NO	Is it known to be an animal pathogen? YES/NO	Is it known to be a zoonotic agent? YES/NO	Maximum quantity to be cultured at one time? (in Litres)	Source/ Supplier	PHAC or CFIA Containment Level
tobacco mosaic virus	☐ Yes ☒ No	☐ Yes ☒ No	☐ Yes ☒ No	**10 mg**	**Dr. Lewis, U Alberta**	☒ 1 ☐ 2 ☐ 2+ ☐ 3
cowpea mosaic virus	☐ Yes ☒ No	☐ Yes ☒ No	☐ Yes ☒ No	**10 mg**	**Dr. Lewis, U Alberta**	☒ 1 ☐ 2 ☐ 2+ ☐ 3
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No			☐ 1 ☐ 2 ☐ 2+ ☐ 3
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No			☐ 1 ☐ 2 ☐ 2+ ☐ 3
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No			☐ 1 ☐ 2 ☐ 2+ ☐ 3
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No			☐ 1 ☐ 2 ☐ 2+ ☐ 3
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No			☐ 1 ☐ 2 ☐ 2+ ☐ 3
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No			☐ 1 ☐ 2 ☐ 2+ ☐ 3

***Please attach a Material Safety Data Sheet or equivalent from the supplier if the bacterium used is not on this link:**
http://www.uwo.ca/humanresources/docandform/docs/ohs/CFIA_Ecoli_list.pdf

Additional Comments: **MSDS is not available**

2.0 Cell Culture

2.1 Does your work involve the use of cell cultures? ☒ YES ☐ NO
(If NO, please proceed to Section 3.0)

2.2 Please indicate the type of primary cells (i.e. derived from fresh tissue) that will be grown in culture:

Cell Type	Is this cell type used in your work?	Source of Primary Cell Culture Tissue	AUS Protocol Number
Human	☐ Yes ☒ No		Not applicable
Rodent	☐ Yes ☒ No		
Non-human primate	☐ Yes ☒ No		
Other (specify)	☐ Yes ☒ No		

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	☒ Yes ☐ No	**See Appendix**	**1**	**ATCC**
Rodent	☐ Yes ☒ No			
Non-human primate	☐ Yes ☒ No			
Other (specify)	☐ Yes ☒ 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 ☒ 1 ☐ 2 ☐ 2+ ☐ 3

Additional Comments: **See Appendix for list of cell lines and information pages**

3.0 Use of Human Source Materials

3.1 Does your work involve the use of human source materials? ☐ YES ☒ 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		☐ Yes ☐ Unknown		☐1 ☐2 ☐2+ ☐3
Human Blood (fraction) or other Body Fluid		☐ Yes ☐ Unknown		☐1 ☐2 ☐2+ ☐3
Human Organs or Tissues (unpreserved)		☐ Yes ☐ Unknown		☐1 ☐2 ☐2+ ☐3
Human Organs or Tissues (preserved)		Not Applicable		Not Applicable

Additional Comments: _____

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? ☐ YES ☒ NO If **NO**, please proceed to Section 5.0

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

Bacteria Used for Cloning *	Plasmid(s) **	Source of Plasmid	Gene Transformed or Transfected	Will there be a change due to transformation of the bacteria?	Will there be a change in the pathogenicity of the bacteria after the genetic modification?	What are the consequences due to the transformation of the bacteria?

** Please attach a Material Safety Data Sheet or equivalent if available.*
*** Please attach a plasmid map.*
****No Material Safety Data Sheet is required for the following strains of E. coli:*
http://www.uwo.ca/humanresources/docandform/docs/ohs/CFIA_Ecoli_list.pdf

4.3 Will genetic modification(s) of bacteria and/or cells involving viral vectors be made?
☐ YES, complete table below ☐ NO

Virus Used for Vector Construction	Vector(s) *	Source of Vector	Gene(s) Transduced	Describe the change that results from transduction

** Please attach a Material Safety Data Sheet or equivalent.*

4.3.1 Will virus be replication defective? ☐ YES ☐ NO

4.3.2 Will virus be infectious to humans or animals? ☐ YES ☐ NO

4.3.3 Will this be expected to increase the containment level required? ☐ YES ☐ NO

5.0 Will genetic sequences from the following be involved?

- HIV ☒ NO ☐ YES, specify
- HTLV 1 or 2 or genes from any Level 1 or Level 2 pathogens ☒ NO ☐ YES, specify
- SV 40 Large T antigen ☒ NO ☐ YES
- E1A oncogene ☒ NO ☐ YES
- Known oncogenes ☒ NO ☐ YES, specify
- Other human or animal pathogen and or their toxins ☒ NO ☐ YES, specify

5.1 Is any work being conducted with prions or prion sequences? ☒ NO ☐ YES

Additional Comments: _____

6.0 Human Gene Therapy Trials

6.1 Will human clinical trials be conducted involving a biological agent? ☐ YES ☒ NO
(including but not limited to microorganisms, viruses, prions, parasites or pathogens of plant or animal origin)
If no, please proceed to Section 7.0

6.2 If YES, please specify which biological agent will be used:
Please attach a full description of the biological agent.

6.3 Will the biological agent be able to replicate in the host? ☐ YES ☐ NO

6.4 How will the biological agent be administered?

6.5 Please give the Health Care Facility where the clinical trial will be conducted:

6.6 Has human ethics approval been obtained? ☐ YES, number: ☐ NO ☐ PENDING

7.0 Animal Experiments

7.1 Will live animals be used? ☐ YES ☒ NO If **NO**, please proceed to section 8.0

7.2 Name of animal species to be used

7.3 AUS protocol #

7.4 List the location(s) for the animal experimentation and housing.

7.5 Will any of the agents listed in section 4.0 be used in live animals
☐ NO ☐ YES, specify:

7.6 Will the agent(s) be shed by the animal:
☐ YES ☐ NO, please justify:

8.0 Use of Animal species with Zoonotic Hazards

8.1 Will any animals with zoonotic hazards or their organs, tissues, lavages or other body fluids including blood be used (see list below)? ☐ YES ☒ NO - If **NO**, please proceed to section 9.0

8.2 Will live animals be used? ☐ YES ☐ NO

8.3 If **YES**, please specify the animal(s) used:

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

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

9.0 Biological Toxins and Hormones

9.1 Will toxins or hormones of biological origin be used? ☐ YES ☒ NO If **NO**, please proceed to Section 10.0

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

9.3 What is the LD_{50} (specify species) of the toxin or hormone

9.4 How much of the toxin or hormone is handled at one time*?

9.5 How much of the toxin or hormone is stored*?

9.6 Will any biological toxins or hormones be used in live animals? ☐ YES ☐ NO
If **YES**, Please provide details:

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

Additional Comments: _____

10.0 Insects

10.1 Do you use insects? ☐ YES ☒ NO - If **NO**, please proceed to Section 11.0

10.2 If YES, please give the name of the species.

10.3 What is the origin of the insect?

10.4 What is the life stage of the insect?

10.5 What is your intention? ☐ Initiate and maintain colony, give location:
☐ "One-time" use, give location:

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

10.7 Do you use insects that require a permit from the CFIA permit? ☐ YES ☐ NO
If **YES**, Please attach the CFIA permit & describe any CFIA permit conditions:

11.0 Plants

11.1 Do you use plants? ☐ YES ☒ NO - If **NO**, please proceed to Section 12.0

11.2 If YES, please give the name of the species.

11.3 What is the origin of the plant?

11.4 What is the form of the plant (seed, seedling, plant, tree…)?

11.5 What is your intention? ☐ Grow and maintain a crop ☐ "One-time" use

11.6 Do you do any modifications to the plant? ☐ YES ☐ NO
If yes, please describe:

11.7 Please describe the risk (if any) of loss of the material from the lab and how this will be mitigated:

11.8 Is the CFIA permit attached? ☐ YES ☐ NO
If **YES**, Please attach the CFIA permit & describe any CFIA permit conditions:

12.0 Import Requirements

12.1 Will any of the above agents be imported? ☐ YES, country of origin ☒ NO
If **NO**, please proceed to Section 13.0

12.2 Has an Import Permit been obtained from HC for human pathogens? ☐ YES ☐ NO

12.3 Has an import permit been obtained from CFIA for animal or plant pathogens? ☐ YES ☐ NO

12.4 Has the import permit been sent to OHS? ☐ YES, please provide permit # ☐ NO

13.0 Training Requirements for Personnel Named on Form

All personnel named on the above form who will be using any of the above named agents are required to attend the following training courses given by OHS:

- Biosafety
- Laboratory and Environmental/Waste Management Safety
- WHMIS (Western or equivalent)
- Employee Health and Safety Orientation

As the Principal Investigator, I have ensured that all of the personnel named on the form who will be using any of the biological agents in Sections 1.0 to 9.0 have been trained.

An X in the check box indicates you agree with the above statement... ☒
Enter Your Name Dr. Leonard Luyt ***Date:*** 10Dec2012

14.0 Containment Levels

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

14.2 Has the facility been certified by OHS for this level of containment?
☒ YES, location and date of most recent biosafety inspection: **Dec 3, 2012**
☐ NO, please certify
☐ NOT REQUIRED for Level 1 containment

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

15.0 Procedures to be Followed

15.1 Are additional risk reduction measures necessary beyond containment level 1, 2, 2+ or 3 measures that are unique to these agents? ☐ YES ☒ NO
If **YES** please describe:

15.2 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:
Staff have been trained to do the following: get immediate medical attention at either LHSC Occupational Health and Safety or Victoria Emergency, visit Occ Health as soon as possible, and file an LHSC incident report. UWO employees are asked to visit UWO Occ Health to file an incident report

15.3 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.shs.uwo.ca/workplace/workplacehealth.html

An X in the check box indicates you agree with the above statement... ☒
Enter Your Name **Dr. Leonard Luyt** *Date:* **10Dec2012**

15.4 Additional Comments: _____

16.0 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: _____
Date: Dec 13, 2012

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

Special Conditions of Approval:

------- Original Message --------
Subject:BARF for A3-125, Vic
Date: Mon, 10 Dec 2012 15:37:57 -0500
From: Len Luyt <lluyt@uwo.ca>
To: Jennifer Stanley <jstanle2@uwo.ca>

Hi Jennifer,

Attached is a BARF for our own facilities. Our radiochemistry lab in Victoria Research Labs is now certified as level 2, room # A3-125. The biology is pretty simple: incubation of cells with our radiolabelled peptides and chemistry with the plant nanoparticles. This relates to my NSERC discovery grant and the renewal that I recently submitted, and also to our Prostate Cancer grant (thus is separate work from the other team grants). Please let me know if there are any issues or changes required.

Thank you,
Len

--
Len Luyt, Ph.D.
Assistant Professor, University of Western Ontario
Scientist, London Regional Cancer Program
http://publish.uwo.ca/~lluyt/

-------- Original Message --------
Subject: Fwd: Fwd: BARF for A3-125, Vic
Date: Wed, 12 Dec 2012 17:51:20 -0500
From: Jennifer Stanley <jstanle2@uwo.ca>
To: Leonard G Luyt <lluyt@uwo.ca>

Hi Dr. Luyt -

I have a couple of questions.

I think the following descriptions were used for the AUP, are these accurate?
CMPV - Cowpea Mosaic Virus, is a plant virus that forms a 31 nm-diameter icosahedral nanoparticle.
TMV - Tobacco Mosaic Virus from tobacco plant, is a virus nanoparticle safe to human and animals.

I am wondering why Section 7.0 is no, I understood from the AUS office that you were planning on using them in animals.

Regards,
Jennifer

-------- Original Message --------
Subject: Fwd: Fwd: Fwd: BARF for A3-125, Vic
Date: Wed, 12 Dec 2012 17:56:59 -0500
From: Jennifer Stanley <jstanle2@uwo.ca>
To: lluyt@uwo.ca

Hi Dr. Luyt

I noticed that Table 2.3 mentions an appendix, that I don't have.

Please clarify.

Jennifer

Subject: UWO : Containment Level???
From: Import Permit Office - Plant Health <PermitOffice@inspection.gc.ca>
Date: 11/1/2012 11:35 AM
To: jstanle2@uwo.ca

Good morning,

Request:
Jennifer Stanley <jstanle2@uwo.ca> 10/31/2012 3:11 pm
CMPV - Cowpea Mosaic Virus
TMV - Tobacco Mosaic Virus

Please let me know the containment requirements for these.

ANSWER:

Tobacco mosaic virus is widespread in Canada, therefore, only a basic containment level is required for this virus.

Cowpea mosaic virus has never been reported in Canada. I do not know the proposed research from the importer, since plants from several (3-9) families are susceptible to the virus, it requires a PPC-1 containment.

Regards,

Import Permit Office/Bureau des permis
Canadian Food Inspection Agency/Agence canadienne d'inspection des aliments
permitoffice@inspection.gc.ca
Telephone: 613-773-7361
Fax: 613-773-7229