CBE/GMO/CBE04

FORM LU/HE/BRA

Version DRAFT 3.0 Aug 08

RISK ASSESSMENT OF WORK WITH BIOLOGICAL MATERIALS

Please note the following before completing this form:

1. University Health and Safety Policy requires that risk assessment of all work with biological materials must be carried out in advance of work commencing. A key requirement of The Control of Substances Hazardous to Health Regulations (COSHH) is to assess the risks associated with any work activity involving the use of biological materials that may contain biological agents.
2. YOU SHOULD COMPLETE ALL OF PART A, THE APPROPRIATE SECTION(S) OF PART B, AND ALL OF PART C. THIS FORM SHOULD BE SUBMITTED TO THE HEALTH AND SAFETY UNIT FOR REVIEW (VIA YOUR DEPARTMENTAL SAFETY OFFICER)
3. It is the responsibility of the Principal Investigator to ensure compliance to these requirements and that this risk assessment remains valid.
4. This risk assessment form **IS NOT** for assessing the risks associated with **Genetically Modified Organism activities**.

Date Submitted:	04/07/2008	Date Approved:	17/09/2008

PART A: Please provide the following general information:

School/Department			
Healthcare Engineering, Wolfson School of Mechanical & Manufacturing Engineering			
The Project			
Title of Project: Single Client Automation Project: ReNeuron			
Project Reference Number: Not Applicable			
Person responsible for this work (*Principle Investigator*):			
Name: Dr Rob Thomas		Position: Lecturer	
Department: Healthcare Engineering		University School: Wolfson School of Mechanical and Manufacturing Engineering	
Person conducting this assessment			
Name: Dr Rob Thomas		Position: Lecturer	
Department:	Healthcare Engineering	Date Risk Assessment Undertaken:	08.07.08
Proposed Project Start Date:	01.08.08	Proposed Project End Date:	01.08.09

Assessment Review:
required at least once a year or immediately following any significant change to the project

	Review 1	Review 2	Review 3	Review 4
Due Date				
Date Conducted				

A1 PROJECT SUMMARY

A1.1 Scientific Goals of the Project *Brief yet clear outline only*

To demonstrate the feasibility of automated processing of a commercial clinically important cell line derived from human foetal neural tissue (CTX0E03).

A1.2 Description of the Experimental Procedures

Describe laboratory procedures to be used and highlight any non-standard laboratory operations

Lyophilised cells will be defrosted, seeded in the Class II hood, cultured (passaged and fed) in the CompacT SelecT, harvested, refrozen, and assessed by flow cytometry. All procedures will be conducted in accordance with the laboratory Quality Management System (QMS) requirements and Code of Practice (COP).

PART B: Please provide information in one or more of the following sections, as appropriate. Only sections which you complete should be submitted:

Section 1: *micro-organisms (prions, viruses, bacteria, fungi, parasites in ACDP category 2 and pathogens controlled by the Department for the Environment, Food and Rural Affairs).* ***[Work with ACDP category 3 and 4 pathogens is not currently permitted in the University.]***

Section 2: *cell cultures, tissues, blood, body fluids or excreta*

Section 3: *plants and plant material*

Section 4: *animals and animal tissues*

SECTION 1: MICRO-ORGANISMS

B1.1 HAZARD AND RISK IDENTIFICATION: NATURE OF MICRO-ORGANISMS

*This information gives an indication of the **potential** harm that the biological material may cause*

B1.1.1 List all micro-organisms to be used

Name	Strain	ADCP cat*	Source

see The Approved List of Biological Agents – available on the Health & Safety website

B1.1.2 Has any strain been genetically modified in any way?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If Yes, complete Genetically Modified Organisms (GMO) Risk Assessment Form	

B1.2 DESCRIPTION OF RISK TO HUMANS

B1.2.1 The disease(s) caused to humans

Describe the type and severity of effects or disease(s) on human health (including colonisation, infection, allergy, toxin-mediated disease) by each of the agents or strains to be used

Indicate in the adjacent box if Not Relevant (N/R)		
Name	Type	Severity

B1.2.2 What is the likelihood of infection of this material? Indicate as None, Low Risk, Medium Risk, High Risk, Known Infected

Name of agent	Risk Category	Justification for Selection
		If none proceed to section B1.3

B1.2.3 Infectivity to humans

Describe ALL the route(s)of infection (relevant to the laboratory setting) and the minimum infectious dose(s) if known (eg percutaneous, mucocutaneous, inhalation, ingestion)

Name of agent(s)	**Route(s) of infection**	**Minimum infectious dose**

B1.2.4 Drug resistance

Is there any known or suspected drug resistance amongst the strains to be used? Identify & describe.

B1.2.5 Attenuation or increased virulence
Are the strains attenuated or do they have an increased virulence in any way?

Identify and describe:

B1.2.6 Ability to survive
In what form is the agent present eg spores or vegetative bacteria, and are there any issues about the agents robustness, including any resistance to chemical disinfectants?

Identify and describe:

B1.2.7 Most hazardous procedure?
Identify and describe the most hazardous procedure(s) to be used.

B1.3 HUMANS AT INCREASED RISK OF INFECTION

B1.3.1 Are there any pre-existing medical conditions that increase the risk associated with this agents listed in section 1.1 (including immunocompromised workers, pregnant workers, breast feeding mothers, diabetic workers)?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, Occupational Health must be consulted:	

B1.4. PROPAGATION OR CONCENTRATION OF ADVENTITIOUS AGENTS

B1.4.1 Give details of the volumes and concentrations of organisms to be used

Name & Strain	Volume	Concentration

B1.5 ENVIRONMENTAL CONSIDERATIONS:

B1.5.1 Are any of the agents capable of causing disease or other harm in animals, fish or plants?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, describe briefly here (A separate risk assessment may be required if the agent to be used poses a significant risk to the environment):	

B1.5.2 Will there be any other environmental risks?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, describe briefly here (NOTE: A separate risk assessment may be required if the agent to be used poses a significant risk to the environment):	

B1.6 OTHER HAZARDS

B1.6.1 Are there any other hazards associated with this work? For example, hazardous chemicals, cryogenic gases ionising radiation.

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, identify these:	
If yes, have these been risk assessed and any necessary approval obtained?	

SECTION 2: CELL CULTURES, TISSUES, BLOOD, BODY FLUIDS OR EXCRETA

B2.1 HAZARD AND RISK IDENTIFICATION: NATURE OF CELLS, TISSUES OR BODY FLUIDS

*This information gives an indication of the **potential** harm that the biological material may cause*

B2.1.1 List all cells or tissues to be used. *For cells indicate if primary, continuous or finite.*

Indicate in the adjacent box if Not Relevant (N/R)			
Cell or tissue type and ID	Organ Source	Species	From where will it be obtained?
CTX0E03 neural stem cells	Foetal neural tissue	Human	ReNeuron, Guilford, UK

B2.1.2 List all blood, body fluids or excreta to be used

Indicate in the adjacent box if Not Relevant (N/R)			N/R
Material type and ID	Organ Source	Species	From where will it be obtained?

B2.1.3 Has any material listed in section B2.1.1 been genetically modified in any way?

Indicate in the adjacent box as No; Yes or Not Relevant (N/R)	YES
If Yes, complete Genetically Modified Organisms (GMO) Risk Assessment Form SEE ATTACHED	

B2.1.4 Will material be screened for infectious agents (if from a cell culture collection answer B2.1.6)?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	YES
This is a clonal cell line that has been comprehensively screened for infectious agents as described in the attached ReNeuron Risk Assessment.	

B2.1.5 Will any clinical history (if relevant) be provided with this material?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	N/R
If yes give details:	
If yes, will a policy of rejection of samples from diseased patients be adopted? Explain	
If yes, how will the information be disseminated in the course of the project?	
If yes, will this information be anonomised?	

B2.1.6 If obtained from a cell culture collection, is safety information provided?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	N/R
If Yes, summarise here:	

B2.2 RISK TO HUMANS

B2.2.1 What is the likelihood of infection of this material? Indicate as None, Low Risk, Medium Risk, High Risk, Known Infected*

Cell type and ID	Risk Category	Justification for Selection
CTX0E03 neural stem cells	Low	Cells screened as described in section B2.14
		If low risk or none proceed to section B2.2.4

see The Managing the risks in laboratories and healthcare premises – available at
http://www.hse.gov.uk/biosafety/biologagents.pdf

B2.2.2 If medium or high risk (section B2.2.1), name and classify the Biological Agents this material could be infected with. List the biological agents and indicate the ACDP hazard group classification*

Name of Agent	Classification

see The Approved List of Biological Agents – available on the Health & Safety website or
http://www.hse.gov.uk/pubns/misc208.pdf.

B2.2.3 Describe the routes of infection (in humans) for these adventitious agents (place a 'X' in the relevant box)

Percutaneous	Mucocutaneous	Inhalation	Ingestion	N/R
Details:				

B2.2.4 Are there any other biological hazards (other than adventitious infectious risk) associated with the materials e.g. tumourogenic cells

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If Yes, describe:	

B2.3 HUMANS AT INCREASED RISK OF INFECTION

B2.3.1 Do any of the agents listed in section B2.1 present an overt risk to humans at increased risk (including immunocompromised workers, pregnant workers, breast feeding mothers)?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If yes, Occupational Health must be consulted:	

B2.4. PROPAGATION OR CONCENTRATION OF ADVENTITIOUS AGENTS

B2.4.1 Will any culturing of this material take place?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	YES
If yes, identify the cells and the conditions these will grow: CTX0E03 neural stem cells cultured in T175 flasks in cell culture media in a 37 degree Celsius humidified incubator	

B2.4.2 If culturing, will CD4+ cells be present. Describe what cells and for how long these cultures will be allowed to grow

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If yes, explain:	

B2.4.3 If culturing, what is the maximum volume of culture grown?

Indicate in the adjacent box if Not Relevant (N/R)	
Per Flask: ~10 million	Per experiment: ~200 million (20 flasks)

B2.4.4 Will the cells be manipulated in any way that could result in a concentration of any adventitious biological agent present?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If yes, explain:	

B2.5 WORKING WITH MATERIAL DONATED BY YOURSELF OR COLLEAGUES : Persons MUST NOT work with their own cells.

B2.5.1 Will any cells be donated by persons working in or has access to the lab?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If yes, explain what precautions are to be taken to prevent that person being exposed to the cells:	
If yes, where will this material be collected:	
If yes, provide justification for not using a safer source:	
If yes, how will confidentiality be assured:	
If yes, has Ethics Committee approval been obtained:	

B2.6 ENVIRONMENTAL CONSIDERATIONS:

B2.6.1 Are any of the agents capable of causing disease or other harm in animals, fish or plants?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If yes, describe:	

B2.6.2 Will there be any other environmental risks?

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	NO
If yes, describe:	

B2.7 OTHER HAZARDS

B2.7.1 Are there any other hazards associated with this work? For example, hazardous chemicals, cryogenic gases ionising radiation.

Indicate in the adjacent box as: Yes, No or Not Relevant (N/R)	YES
If yes, identify these: Cryogenic processing with liquid nitrogen	
If yes, have these been risk assessed and any necessary approval obtained? Procedures in accordance with SOP013, 2Use and Maintenance of Liquid Nitrogen Stores". Risk Assessment Reference: SAF/MM/1638	

SECTION 3: PLANTS, PLANT TISSUE OR MATERIAL, PLANT PATHOGENS

B3.1 HAZARD AND RISK IDENTIFICATION: NATURE OF PLANT, PLANT TISSUE OR MATERIAL, PLANT PATHOGENS

This information gives an indication of the **potential** harm that the biological material may cause

B3.1.1 List all plant or plant tissues to be used

B3.1.2 Is any of the material listed in B3.1.1 infected with pathogen?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, also complete Section 1	

B3.1.3 Is any material listed in B3.1.1 transgenic?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If Yes, complete GM Risk Assessment Form	

B3.2 RISK TO HUMANS

B3.2.1 The disease(s) caused to humans

Describe the type and severity of effects or disease(s) on human health (including irritation, allergy, effect of toxins) by each of the materials to be used

Name of plant/plant tissue	Type	Severity

B3.2.2 What is the likelihood of infection of this material? Indicate as None, Low Risk, Medium Risk, High Risk, Known Infected

Name of plant/tissue	Risk Category	Justification for Selection
		If none proceed to section B3.3

B3.2.3 Describe the routes of that the effects described in section B3.2.1 are transmitted (place a 'X' in the relevant box)

Percutaneous	Mucocutaneous	Inhalation	Ingestion	N/R
Details:				

B3.3 HUMANS AT INCREASED RISK OF INFECTION

B3.3.1 Do any of the agents listed in section 4.1 present an overt risk to humans at increased risk (including immunocompromised workers, pregnant workers, breast feeding mothers)?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, Occupational Health must be consulted:	

B3.4 ENVIRONMENTAL CONSIDERATIONS: Risk to other plants

B3.4.1 Will there be any risk other plants?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, describe:	

B3.4.2 Will there be any other environmental risks?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, describe:	

B3.4.3 Is the plant to be used controlled by the Department for the Environment, Food and Rural Affairs?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, approval will not be granted until a copy of the DEFRA licence has been submitted to the Biological Safety Group:	

B3.5 OTHER HAZARDS

B3.5.1 Are there any other hazards associated with this work? For example, hazardous chemicals, cryogenic gases ionising radiation.

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, identify these:	
If yes, have these been risk assessed and any necessary approval obtained?	

SECTION 4: ANIMALS AND ANIMAL TISSUES

B4.1 HAZARD AND RISK IDENTIFICATION: NATURE OF ANIMALS OR TISSUE

*This information gives an indication of the **potential** harm that the biological material may cause*

B4.1.1 List all animals or animal tissues to be used

Species	Sex	Source	Anatomical Site	Origin or geographical source

B4.1.2 Is the animal or tissue/body fluid to be worked with infected or to be infected?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If Yes, complete Section 1 of this form	

B4.1.3 Is a carcinogen, drug or other substance to be administered to the animal(s) or present in the tissue?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If Yes, complete the appropriate Chemical COSHH Assessment	

B4.1.4 Have the investigators that will be performing the work on animals obtained the appropriate Home Office Licence?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If No, consult the H&S Office.	

B4.1.5 Have Standard Operating Procedures (SOPs) for the proposed work been approved?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If No, consult the H&S Office. If Yes attach the signed approval.	

B4.2 RISK TO HUMANS

B4.2.1 The disease(s) caused to humans

Describe the type and severity of effects or disease(s) on human health (including infection, allergy, bites and scratches)

Name of animal/animal tissue	Type	Severity

B4.2.2 What is the likelihood of infection of this material? INDICATE as None, Low Risk, Medium Risk, High Risk, Known Infected

Name of agent	Risk Category	Justification for Selection
		If none proceed to section B4.3

B4.2.3 Describe the routes of that the effects described in section B4.2.1 are transmitted (place a 'X' in the relevant box)

Percutaneous	Mucocutaneous	Inhalation	Ingestion	N/R
Details:				

B4.3 HUMANS AT INCREASED RISK OF INFECTION

B4.3.1 Do any of the agents listed in section B4.1 present an overt risk to humans at increased risk (including immunocompromised workers, pregnant workers, breast feeding mothers, workers repeatedly handling or multiply dosing animals)?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, Occupational Health must be consulted:	

B4.4. PROPAGATION OR CONCENTRATION OF ADVENTITIOUS AGENTS

B4.4.1 Will any culturing of this material take place?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, complete Section 2 of this form:	

B4.4.2 How many animals will be used?

Indicate in the adjacent box if Not Relevant (N/R)	

B4.5 ENVIRONMENTAL CONSIDERATIONS: Risk to other animals

B4.5.1 Will there be any risk other animals?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	

If yes, describe:

B4.5.2 Will there be any other environmental risks?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	
If yes, describe:	

PART C: CONTROL MEASURES

C1. CONTROL MEASURES

The risk of exposure must be prevented or adequately controlled to minimise the chance of harm arising. COSHH Regulations require minimum containment measures for laboratories handling organisms from the different ACDP hazard groups (http://www.hse.gov.uk/pubns/misc208.pdf)
The hazard group number typically indicates the level of containment (includes physical measures & working practices) that must be used for its handling).

C1.1 Preventing Exposure

C1.1.1 Substitution with a Safer Alternative

Is substitution with a safer alternative practical, by for example, replacement of a clinical strain or pathogen with one that is lab adapted? Provide reasons for your answer:

No. This is a clinical cell line and is specific material supplied by the partner for this work

C1.1.2 Isolation/Segregation

(i) Is/Are the laboratory(s) to be used for this work to be shared with other workers not directly involved in this activity?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	YES
If yes, provide details: Access restricted to authorised lab workers with appropriate training in accordance with documented the COP and QMS requirements for Class II work	

(ii) Is access to the laboratory(s) to be used for this work restricted?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	YES
If yes, provide details: Restricted to people with appropriate training (authorised access documented in individual training records) in accordance with the COP and QMS	

C1.2 Controlling Exposure

C1.2.1 Are sharps (needles, blades, scissors, forceps, glass or capillary tubes) to be used at any stage during this activity?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO
If yes, list the sharps:	
If yes, justify there use – is there an alternative?:	
If yes, describe there use and disposal:	

If yes, describe any additional precautions employed to reduce risk:

C1.2.2 Containment and Ventilation

(i) Is the use of BSC required for the protection of the worker ie do the work procedures generate aerosols or splashes that pose a risk to workers?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	YES
If yes, specify the type(s) and when they will be used: A Class II Biological Safety Cabinet will be used for all manipulations according to SOP 1) SOP009, "Use and Maintenance of BSC-G2000 Vertical Laminar Airflow Cabinet" 2) SOP052, "Use and Maintenance of Bioquell Class II Cabinet" 3) SOP035, "Use and Maintenance of CompacT SelecT"	
(ii) Are there any requirements for room ventilation e.g. negative pressure, temperature control?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO
If yes, specify:	

C1.2.3 Transport and Storage within the laboratory

How and where are materials to be stored? Material will be stored in a cryobank or temporary storage in designated cell culture incubators according to the following SOPs : 1) SOP005, "Storage and Transport of Biological Agents" 2) SOP013, "Use and maintenance of Liquid Nitrogen Stores" 3) SOP017, "Use and maintenance of the Galaxy-R Incubator" 4) SOP031, "Cryopreservation and Storage of Mammalian Cell Lines" 5) SOP053, "Use and maintenance of the Sanyo CO2 Incubator"
How will this material be transported within the laboratory e.g. between BSC and incubator? Detail the containment measures which will be used to prevent or contain accidental splashes or spills. Cells will always be transferred in closed containers. Appropriate spill response procedures are posted in the lab and documented in detail in the following SOPs: 1) SOP005, "Storage and Transport of Biological Agents" 2) SOP038, "Biological Spill Response"

C1.2.4 Local transport out of the laboratory

How will this material be transported on-site (e.g. research material between labs on campus or movement of waste containing viable agents e.g. to a remote autoclave? Detail the containment measures which will be used to prevent or contain accidental splashes or spills

Transfer outside the laboratory is not anticipated but any requirement is likely to be constrained within the Wolfson building. If necessary, transfers will use double containment procedures Transport of research material between laboratories is done using sealed containers which are put into tube racks and trays and transported using trolleys according to the following SOPs. Waste potentially containing viable agents is not removed from the laboratories until it has been autoclaved ie autoclaves are not remotely situated.

1) SOP003, "Disposal and Disinfection of Biological Waste"
2) SOP005, "Storage and Transport of Biological Agents"
3) SOP038, "Biological Spill Response"

C1.2.5 Shipment of Biological Material

*Will this material be shipped elsewhere in the UK or abroad?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	YES

If yes, give details to support compliance to the relevant regulation (e.g. category of material, correct packaging instruction):

This is 'Category B' material and will be packaged in compliance with the full guidelines found at the HSE website below. In short this includes a leak proof inner receptacle, a secondary container secured in cushioning and absorbent material sufficient to absorb the entire contents of the inner receptacle, and an outer container. The packaging will be robust enough to withstand a drop of at least 1.2 metres and will be marked externally with a black diamond containing the identifier 'UN 3373'.

see The Managing the risks in laboratories and healthcare premises – available at
http://www.hse.gov.uk/biosafety/biologagents.pdf

If material will be received from other sites or organisations, what precautions are being taken to ensure that the material is shipped correctly?

The material will be shipped from ReNeuron according to their own Quality Management procedures. The procedure for the safe receipt of packages containing potentially biohazardous material and their delivery to the appropriate recipient or other designated personnel is documented in SOP008; "Receipt of Purchased Biohazardous Material. This SOP is intended to minimize the consequences that could result from the failure of packaging methods and materials used to ship biohazardous materials.

C1.2.7 Centrifugation

(i) If material is to be centrifuged will sealed buckets and rotors be used?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	YES

(ii) Where will these rotors/buckets be opened?

Centrifuge is operated and maintained according to SOP015 and SOP038. Sealed buckets will be opened within the Class II laboratory environment according to the following SOPs

1) SOP009, "Use and Maintenance of BSC-G2000 Vertical Laminar Airflow Cabinet"
2) SOP052, "Use and Maintenance of Bioquell Class II Cabinet"

(iii)Describe the procedures in place to deal with leaks and spillages in the centrifuge

Procedures to prevent, contain and respond to leakages and spillages in the centrifuge are detailed in the following SOPs:

1) SOP015, "Use and maintenance of BOECO U032R Centrifuge"
2) SOP038, "Biological Spill Response"

Posters are also displayed around the laboratory to advise on spillages.

C1.2.8 Incubators

If incubators are to be used, what type of incubator (e.g. shaking, static) is used and describe procedures to prevent and contain spillages.

Static incubators are used. Procedures to prevent, contain and respond to spillages in the incubators are detailed in the following SOPs:

1) SOP017, "Use and maintenance of the Galaxy-R Incubator"
2) SOP038, "Biological Spill Response"
3) SOP053, "Use and maintenance of Sanyo C02 Incubator"

C1.2.9 Disinfection

Specify the type and concentration of disinfectants to be used:

The disinfectants were carefully chosen for effectiveness in use. The number of disinfectants in use is strictly limited to avoid errors and ambiguities in use and accidental mixing of compounds that may give rise to hazardous reactions or the formation of toxic products. Unless there are compelling reasons to do otherwise, Virkon (1% w/v) is the sole disinfectant used in the T208/T207 laboratories other than 70% IMS which is used used for general disinfection cleaning (SOP004) where Virkon cannot be used.

Virkon has a wide range of bactericidal, virucidal, fungicidal and sporocidal activities. Representative viruses from all the major virus families are inactivated by Virkon. Working solutions of 1% w/v have low toxicity and no irritancy. Selection and procedures detailed in the following SOPs:

1) SOP004 General Laboratory Maintenance and cleaning
2) SOP006 Selection and Use of Disinfectants
3) SOP039 Storage, Handling and Disposal of Chemicals

Have these disinfectants been validated for use with the recipient biological material?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO

If yes, describe the procedure:

For Hazard Group 1 and 2 Biological agents it is normally be sufficient to rely on the manufacturers data, providing the recommended concentrations and contact times are used. Hence Virkon (1%) is used as per manufacturers instruction and according to standard procedures detailed in the COP and the following SOP:

1) SOP006, "Selection and Use of Disinfectants"

C1.2.10 Personal Protective Equipment (PPE)

(i) What type of lab coats will be worn and where will they be stored?

Various sizes of rear fastening lab coats are worn which have elasticated cuffs. They are stored outside the laboratory.foyer. Proper use of PPE is described in the following SOP: SOP037, "Use of Personal Protective Equipment"

(ii) What type of gloves will be worn and where will they be stored?

1. Autoclave gloves, which will be stored in close proximity to the autoclave equipment
2. Cryogenic gloves, which will stored in close proximity to the Liquid Nitrogen storage containers
3. Latex powder free gloves for general use, which will be stored in the laboratory

Correct use of PPE is described in the following SOP: SOP037, "Use of Personal Protective Equipment"

(iii) Describe any other PPE to be used:

1. Laboratory safety glasses (including those for spectacle wearers)
2. Face Shields (primarily for handling liquid nitrogen)
3. Shoe covers, in case of a spillage
4. Aprons or disposable lab coats for extra protection over laboratory coat.

Correct use of the above PPE is described in the following SOP: SOP037, "Use of Personal Protective Equipment"

C1.2.11 Hygiene Measures

Describe the hygiene facilities available and where they are located

1) Eye Wash station located in the laboratory foyer
2) Hand washing facilities located in the laboratory foyer

C1.2.12 Vaccination

Are effective vaccines available against any of the agents listed in Section1, 2, 3, or 4 of Part B?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO
If yes, describe:	

C1.2.13 Waste Treatment before Disposal

How must waste to be treated before disposal and how has it been validated as being effective?

	Treatment before disposal	Validation
Liquid waste	Virkon sterilise (SOP003 – disposal and disinfection of biological waste)	According to manufacturers instructions; see section C2.1.9
Solid waste	Autoclave sterilise (SOP003 – disposal and disinfection of biological waste)	Treatment Cycle periodically validated according to SOP 010

C1.2.14 Autoclave sterilisation

If waste is treated by autoclave sterilisation then this section must be completed. If this section is not relevant then hatch the box

	Type of waste	*Autoclave cycle (temp, cycle time)*	*Treatment monitor*
Liquid waste			

Solid waste	Cell Culture consumables	121°C for 1 hour	Designated Autoclave tape monitors
Location of autoclave	*Servicing details*	*Location of back-up autoclave*	*Designated area for storage of unsterilised waste*
Laboratory T208B ie same location as intended work	Annual	Laboratory T207	On designated benches adjacent to the autoclave

C1.2.15 Liquid Waste Disposal

How will liquid waste be disposed of?
To the drain? Yes: with copious amounts of water in accordance with SOP003 – "Disposal and disinfection of biological waste"
As solid waste? No
Other? None

C1.2.16 Solid Waste Disposal

Describe the waste category and disposal route. *(For guidance refer* to http://www.environment-agency.gov.uk). **Hatch the relevant Box(es)**.

European Waste Catalogue Code	Categorisation		Disposal Method
		Hatch relevant box(es)	
18 01 01	Sharps		Sharps bin>autoclave sterilisation if known or potentially infected >clinical waste disposal (incineration)
18 01 02 [human]	Human body parts, organs, including blood bags and blood preserves and excreta (unless identified as medium or high risk or known infected in Section 2.16 of this RA in which case they must be pre-treated before disposal and classified 18 01 04 [sealed bins])		Rigid one way sealed tissue bins>incineration only
18 01 02 [animal]	Animal body carcases or recognisable parts ((unless identified as medium or high risk or known infected in Section 2.16 of this RA in which case they must be pre-treated before disposal and classified 18 01 04 [sealed bins])		Rigid one way sealed tissue bins > incineration only
18 01 03	Potentially or known infected lab wastes (including sharps) of HG2, GM Class 2, DEFRA Cat 2 or higher, that have not been pre-treated before leaving the site.		This is not a route of preference and is subject to special requirements

18 01 04 [bags]	Infected or potentially infected lab wastes that have been pre treated before leaving the site		Disinfection or sterilisation (as identified in C1.2.13) in the lab suite > placement in yellow clinical waste bags > clinical waste disposal (incineration)
18 01 04 [sealed bins]	Infected or potentially infected animal or human body parts, organs or excreta that have been pre treated before leaving site		Disinfection or sterilisation (as identified in C1.2.13) in the lab suite > placement in yellow one way sealed tissue bins > incineration)

C1.2.17 Work with Animals or Vectors (if none proceed to Section C1.2.18)

(i) Are animals or vectors to be infected with any of these biological agents?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	N/R
If yes, describe the procedure and describe where this aspect of the work will be conducted:	
(ii) Is shedding of infectious materials by the infected animals possible or expected?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	N/R
If yes, describe the routes of shedding, risk periods for such shedding and the additional precautions required to control exposure:	
(iii) Who will perform the inoculations of animals/vectors? What training have they received?	
Indicate in the adjacent box if Not Relevant (N/R)	N/R
Provide details of the training required:	

C1.2.18 Bioreactor/Fermenters (if none proceed to Section C1.2.19)

Will a fermenter be used to culture a pathogen?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO
If yes, describe the size, and type of the fermenter.	
(ii) Are any supplementary containment measures required, for example, the use of a BSC or spill tray.	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	N/R
If yes, describe:	

C1.2.19 Other Control Measures Required?

None

C1.3 Emergency Procedures

C1.3.1 Describe the procedures in place for dealing with spillages *(specify disinfectants and any special containment for large volumes)*

Within the BSC:

Procedures for dealing with small and large spillages are detailed in the following SOPs:

1) SOP006, "Selection and use of Disinfectants"
2) SOP009, "Use and Maintenance of BSC-G2000 Vertical Laminar Airflow Cabinet"
3) SOP038, "Biological Spill Response"
4) SOP052, "Use and Maintenance of Bioquell Class II Cabinet"

Posters displayed within the laboratory detail what to do in the event of a spillage

Within the laboratory but outside the control measure e.g. BSC, spill tray

Procedures for dealing with small and large spillages are detailed in the following SOPs:

1) SOP006, "Selection and use of Disinfectants"
2) SOP038, "Biological Spill Response"

Outside the laboratory e.g. during transport

Procedures for dealing with small and large spillages are detailed in the the COP and the following SOPs:

1) SOP005, "Storage and Transport of Biological Agents"
2) SOP006, "Selection and use of Disinfectants"
3) SOP038, "Biological Spill Response"

Describe the procedures in place for an accidental exposure (if necessary describe different procedures for different types of exposure e.g. eye splash or percutaneous inoculation)

Procedures to respond to accidental exposure are detailed in the COP and the following SOP:

1) SOP038, "Biological Spill Response"

C2 ASSIGNMENT OF CONTAINMENT LEVEL

The laboratory Containment Level is directly related to each of the 4 Hazard Groups; organisms categorised as HG1 (lowest hazard rating) should normally be handled in CL1 facilities (minimum level of containment), and likewise up to HG4 (highest hazard rating) in CL4 facilities (maximum level of containment). Where the identity or presence of a biological agent is not known the following rules apply: a) where uncertainty exists over the presence of pathogenic biological agent – minimum of CL2; b) where the presence of a pathogenic biological agent is known or suspected – minimum of Containment Level appropriate to the agent, where the assessment is inconclusive but where the activity might involve serious risk – minimum CL3

C2.1. What containment level is required for this work?

Class I

C2.2. Describe extra controls or derogation from certain controls
:

None

C3 FACILITIES

C3.1 Where will this work take place?

Room(s)	Building	Campus	Person in Control of area
T208B	Wolfson School of Mechanical & Manufacturing Engineering	Loughborough University	Carolyn Thomas Bob Temple

C4 PERSONNEL

C4.1 Names of Personnel involved in the Project

Surname	Initials	Staff ID	Position
Thomas	RT	5007730	Lecturer

C4.2 Information, Instruction and Training

Describe the training that will be given to all those affected (directly or indirectly) by the work activity. Instruction should include the 'Local Rules' or 'Local Codes of Practice' which focus on the working instructions to be followed by all persons involved in the work activity to control or prevent exposure to hazardous biological agent(s). These should be written and readily available to all workers working at Containment Level 2. A formal record of training should be kept for all individuals working at Containment Level 2.

Formal records of training are kept for all workers at containment level II. Instruction against local QMS ie SOPs and the local COP is provided.

C4.3 Relevant Experience/Training:

Surname	Experience/Training
Thomas	Documented in Personal Training File

C4.4 Other people who may be at risk from the activity e.g. cleaners, maintenance workers or other workers in shared laboratory

Details:

None

C5 OCCUPATIONAL HEALTH

C5.1 Vaccination

Is an effective vaccination available for any of the pathogens associated with this work? Advice can be obtained from the Occupational Health Adviser if required. All workers involved with handling unscreened blood, blood products and other tissues are recommended to have Hepatitis B immunization

Certificate for Hepatitis B immunization documented in personal training file.

C5.2 Health Surveillance

Is health surveillance required? (Health surveillance is typically applied if working with a hazardous substance that: a) produces an identifiable disease or adverse health effect that can be related to exposure; b) there is a reasonable likelihood that the disease or effect may occur under the conditions of work, and c) there are valid techniques for detecting indications of the disease or effect).

NO

C6. NOTIFICATIONS: Human Tissue Act

C6.1.1 Relevant material covered by the Human Tissue Act

Are any of the cell, tissues or fluids to be used covered by the Human Tissue Act?	
Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO

C6.1.2 Does This Work Have Ethical Approval? If Yes, Provide Details

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	YES
Approval number: 08/H0406/122	
Date obtained: 19/08.08	Ethics committee name: NHS Research Ethics Committee: Leicestershire, Northamptonshire & Rutland EC1

C6.1.3 Are other registrations/notifications required for this work? For example HSE notification under COSHH, Home Office notification under anti-terrorism, crime and security act etc

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	NO
If Yes, give details:	

7. LICENSING REQUIREMENTS FOR ANIMAL PRODUCTS

C7.1.1 Are there any licensing requirements for this work?

Indicate in the adjacent box as No, Yes or Not Relevant (N/R)	N/R

NOTE: The regulations covering the import of animal products (including tissue cultures, tissues, body fluids or fractions thereof) are in a state of flux. See the DEFRA website for details.

UNLESS THIS SECTION IS NOT RELEVANT (N/R) ie THE INTENDED WORK DOES NOT USE ANIMAL PRODUCTS - CONSULT THE LU H&S OFFICE TO REVIEW APPLICATION REQUIREMENTS BEFORE ANY SUBMISSIONS

8. DECLARATION

*The declaration must be signed **before** submitting this assessment to the Departmental Safety Officer and University Biological Safety Officer*

I, the undersigned:

- confirm that all information contained in this assessment is correct and up to date
- will ensure that **suitable and sufficient instruction, information and supervision** is provided for all individuals working on the activity
- will ensure that no work will be carried out until this **assessment has been completed and approved** and that all necessary control measures are in place
- accept that for some Containment Level 2 and all CL3 activities **a statutory notification period of 20 days** may be required before work can commence
- that all information contained in this assessment must remain correct and up to date (the assessment should be **reviewed once a year** and whenever any **significant changes** to the work activity occur)
- will re-submit the assessment for approval if any significant changes occur

Name: Person conducting assessment	**Signature**	**Date**
R THOMAS	R. Thomas	4/9/08
Name: Principal Investigator	**Signature**	**Date**
R THOMAS	R. S. Thomas	4/9/08

9.APPROVAL

Name: Departmental Safety Officer	**Signature**	**Date**
R I TEMPLE	R I Temple	05/07/08
Name: University Biological Safety Officer	**Signature**	**Date**
C. Moore	C. M. Moore.	17/9/08.

Loughborough University

For Health and Safety Unit Use only ASSESSMENT NO.

RISK ASSESSMENT of WORK with

GENETICALLY MODIFIED ORGANISMS

The requirements of Genetically Modified Organisms (Contained Use) Regulations 2000 are reflected in the University Health and Safety Policy which requires that risk assessment of all work with Genetically Modified Organisms ***must*** *be carried out in advance of work commencing and, in addition,* ***must be scrutinised and approved*** *by the University's relevant Safety personnel. The tables at the end of this document are drawn from the current legislation and the appropriate table* ***must*** *be completed as part of the assessment. Finally,* ***WORK MUST NOT BEGIN*** *until the proposal has been* ***approved*** *and clearance has been given via Health and Safety.*

Date submitted		**Date approved**	

Please provide the following general information:

School/Department	Wolfson School of Mechanical and Manufacturing Engineering

Principal investigator	David Williams	**Position**	Professor Healthcare Engineering
E-mail address	RiJ.Thomas@Lboro.ac.uk	**Phone no.**	7601

Please give a brief and descriptive title for this risk assessment

Title	Culturing genetically modified human neural progenitor cells

Please provide a brief description of the nature of the work, identifying any GMMs produced *(e.g. virus vector with insert)*, and their use to transform cells. Please identify the components of the project for which this risk assessment is carried out.

No GMMs are produced in this project. A GM neural progenitor cell line CTX0E03 is to be obtained from a partner company, ReNeuron, for the purpose of scaleable manufacturing cell culture trials. These cells are undergoing European safety assessment as a advanced therapeutic product. They have been thoroughly evaluated for handling safety by the deriving organisation, ReNeuron, and have been classified as hazard group/containment level 1 i.e. organism presenting 'effectively zero' risk. This risk assessment is attached and should be referred to for the 'characteristics' sections of this RA.

Donor	
Name of gene/nucleic acid sequences	
Vector	
Host	
ACDP category* of host (where appropriate)	

*The ACDP categorisation of biological agents can be found in the *Approved List of Biological Agents* published by the Health and Safety Executive.

Note: The questions in this proforma are designed to ensure that all the relevant issues have been addressed for the majority of Risk Assessments for work involving Genetic Modification at the University of Loughborough. However in the interests of streamlining the majority of applications, and because not all

possible applications of genetic modification may have been anticipated, there may be instances in which answer of these questions alone may not be sufficient for a full risk assessment. The Genetic Modification Safety Committees reserve the right to request additional information. For a more complete description of the requirements of a Risk Assessment, refer to ACGM notes and newsletters, and the Guidelines to the 2000 Regulations. Less detail will be required for commonly used and familiar host/vector systems than for those less widely known or characterised. References may be helpful in some instances.

It may be appropriate to write the assessment to cover a range of closely related GMOs, e.g. a defined family of genes, a range of vectors with similar properties, complete and partial sequences, with and without expression; however the assessment and containment conditions proposed must reflect the greatest potential hazard of any of the range of GMMs covered by the assessment.

Do not feel constrained by the box sizes, in some cases considerably greater amounts of information may be required. The box sizes should expand to accommodate your text. To add further rows to a table, use tab key when cursor is in the last box.

Any potentially confidential information should be highlighted, e.g. by use of **red text**. This will include all personal information, and possibly e.g. commercially sensitive information, which the applicant wishes **NOT TO APPEAR ON THE PUBLIC REGISTER**. NB There are tight restrictions on what will be accepted as confidential. The remainder of the risk assessment must be understandable without the confidential information.

It may be possible for outside bodies to access information in this form under the Freedom of Information Act, unless it can be categorised as an exemption. Furthermore, work with organisms listed in Schedule 5 of the Anti-terrorism, Crime and Security Act 2001, or genetic material from those organisms, may be notifiable to the Home Office.

Characteristics of the Donor, Insert, Vector and Host

Name (species/strain if appropriate) **and characteristics of the source of the nucleic acid sequences ("the donor)**

Note: Species from which the nucleic acid sequences were obtained, whether a pest or pathogen, tissue (normal, tumour, healthy or diseased), health status of the donor, etc.

Name, description and function of the gene/nucleic acid sequences involved ("the insert")

Note: Biological function of the intact, natural gene; whether protein-coding sequence complete, partial, unknown, or known to be absent in construct; whether or not interrupted by introns etc; whether wild type or mutant; known, suspected or intended function of mutants; any other biological activities e.g. antisense, ribozyme, replication origin, mobilisation functions, etc. Genomic or cDNA library (consider the properties of the library as a whole; separate assessment is required for the specific clones you intend to isolate from the library).

Name and characteristics of the "vector"

Note: Name of parental plasmid, bacteriophage, etc; characteristics, i.e. mobilisable, mobilisation defective, non-mobilisable; host range; presence of drug resistance markers or other sequences of potential clinical or environmental significance. Whether constructs transferred into host cells e.g. as non-mobilisable DNA; presence of replication origins, conditional (e.g. SV40, EBV) or otherwise. Involvement of viral vectors (e.g. retrovirus, baculovirus); name, characteristics, whether replication defective and the basis of this (e.g. deletion); host range; pathogenicity; potential for complementation by products expressed in the host, or by superinfection, etc.

Name and characteristics of the "host"

Note: Species/strain etc, whether disabled/ highly disabled; presence of other agents which may e.g. assist transmission; or affect pathogenicity; any history of safe use; whether an intact multicellular organism is produced at any stage (e.g. transgenic animals, plants); if host is (a) cell line(s) derived from multicellular organisms, the species, any potential for harm to humans or the environment; presence of other agents which are themselves transmissible or may assist the mobilisation of the transferred sequences e.g. as a result of recombination.

Characteristics of the Genetically Modified (Micro)Organism

Will there be expression of the protein (or other functional product) encoded by the insert, in the genetically modified organism?

Note: Provide details, e.g. of the promoter, level of expression, secretion, presence of introns within the coding region which might preclude expression of a functional product in E. coli, or other specific hosts, etc.

Specify any known or expected characteristics of the GMO which pose a risk to human health and safety and assess the severity and likelihood of such effects

Effects on human health (include colonisation, infection, allergy, toxin-mediated disease)
Humans at increased risk of the above effects (e.g. immunocompromised, pregnant or breastfeeding women)

Note: Characteristics which might increase the pathogenicity of the GMO relative to the unmodified host, or decrease susceptibility to control measures, e.g. alteration in susceptibility to clinically relevant drugs or to immunological or other natural defences; any other potentially significant biological activities of encoded products, e.g. potential toxicity, allergenicity, growth promotion/inhibition, oncogenicity, other pharmacological activity, etc.

Does this project involve work with animals? Provide details

Either use of transgenic animals or work with GMMs in animal models

Quantity of organisms to be used

Specify volumes and concentrations/culture density

Interim Assignment of Containment Conditions to Protect Human Health

Using the appropriate table(s) in Annex 1 of this form please select your control measures (you may place a **X** alongside each appropriate control measure to indicate that you have considered each one) and assign an interim level of containment for the work, i.e. ACGM containment level, (taking into account the hazard grouping of any biological agent). Please justify your decision to use this level of containment.
NB CLASSIFICATION OF THE PROJECT IS DEPENDENT ON ONLY THOSE CONTROL MEASURES THAT ARE SHOWN BY THE RISK ASSESSMENT TO BE NECESSARY TO PROTECT HUMAN HEALTH OR THE ENVIRONMENT. MEASURES THAT RESULT FROM CONVENTION, CONVENIENCE OR ARE REQUIRED FOR PRODUCT PROTECTION ARE NOT RELEVANT TO THE CLASSIFICATION See ACGM Newsletter 27/ACGM Compendium of guidance for further information

Interim containment level and corresponding Class (classes) of GMO(s) involved in the work (& explanation)

This cells will be handled in class II containment facilities (see attached RA). The cells are less hazardous when modified.

Note: You will need to consider the containment level necessary to control the risk of the host and then make a judgement as to whether the modification will result in a GMO more hazardous/less hazardous/about the same

Please provide the following information for the Committee:

Are any of the work procedures likely to generate aerosols? If so, is the work to be undertaken in a safety cabinet?

Aerosols may be generated when pipetting or manipulating solutions. All such manipulations and vial openings will be conducted in a class II environment

Identify any use of sharps in the work; justify their use and specify control measures

No sharps will be used.

Protective equipment and clothing to be used

Standard laboratory safety equipment will be used. Latex gloves and laboratory over coat.

Transport and storage arrangements

SOP 005 will be followed: Storage and transport of biological agents. Transport outside the laboratory and to the company will use a specialised 'dry shipper' unit provided by ReNeuron.

Specify arrangements for safe storage; whether, and if so how, materials are likely to be transported between buildings, on public roads, or posted)

Disinfection

1% Virkon for liquids as specified in attached ReNeuron RA and SOP 003 Disposal and Disinfection of Biological waste. Solid waste will be autoclaved and sent for incineration.

Specify disinfectant(s) to be used, and their dilution. Have these been validated for use with the relevant organism?

Inactivation of GMMs in waste, and subsequent disposal

1% Virkon for liquids as specified in attached ReNeuron RA and SOP 003 Disposal and Disinfection of Biological waste. Solid waste will be autoclaved and sent for incineration.

The Contained Use Regulations 2000 require that GMMs in contaminated material and waste are inactivated by validated means. You must specify the METHOD of inactivation of the GMMs, the expected DEGREE OF KILL of the GMM achieved by that method, and the VALIDATION of that method.

Monitoring of Containment and Control Methods

Monitoring of containment at point of use

Not required as these cells will not survive outside a highly specialised environment

Monitoring of waste inactivation methods

As in SOP 003 – periodic validation of autoclave

Emergency procedures - Is an emergency plan required? Provide details (or attach)

No

Note: In the event of a reasonably foreseeable accident where the health and safety of people outside the premises is liable to be seriously affected or where there is a serious risk of damage to the environment then an emergency plan is required. This plan may need to be communicated to the emergency services and other relevant bodies. In most cases this will only be required for Class 3 and 4 projects (See ACGM Newsletter 27/Compendium of Guidance for further information). However, details of accident/spillage procedures should be provided for all projects.

Occupational Health issues

None

Specify any requirements for immunisation, chemoprophylaxis or health monitoring, and any special requirements for record keeping

Environmental Considerations

ANSWERS MUST BE JUSTIFIED IN SOME DETAIL, i.e.- IT IS NOT ACCEPTABLE TO SIMPLY STATE THAT THERE IS NO RISK TO THE ENVIRONMENT.

Risk to animals, fish, plants etc

If the recipient microorganism is controlled by DEFRA, do you have a DEFRA licence? (delete as appropriate)	**NA**

Approval will not be granted until a copy of the DEFRA licence (if applicable) has been submitted to both the local GMSC and the Advisory Group for the Control of Biological Hazards

Identify any identifiable potential hazards to the environment, which might occur if the genetically modified organism were to be accidentally released. Classify the potential hazard as Severe, Medium, Low or Negligible.

Negligible – see RA

Note Potential hazards might be identified, and their severity assessed, dependent upon: the host species, the vector or the insert; or phenotypic changes caused by the genetic modification; the presence of host or susceptible species in the environment; the potential for survival, multiplication and dissemination in the environment; the stability of the GMO in the environment; the possibility of gene transfer to other species, etc. Refer to ACGM Compendium of guidance for further information

In view of the characteristics of the GMO, specify the likelihood of accidental release and occurrence of the above mentioned potential harmful effects, if the work were to be performed at the interim containment level specified above. Classify this as High, Medium, Low or Negligible.

Negligible – see RA

Note: This includes the wider as well as the local environment in which the activity is to be carried out. Consideration should be given to any potential exposure of the environment to the GMMs and the magnitude and duration of such exposure. Refer to ACGM guidance for further information

Grade the overall Risk to the environment (= Potential harm x Likelihood) as High, Medium, Low or Effectively Zero.

Effectively Zero – See RA

Additional Containment

If, in considering the potential for harm to the environment, you have concluded that the Risk to the environment is high or medium, then the containment conditions previously specified may need to be modified to reduce the risk to an acceptably low level. Use these considerations to revise your provisional containment level so that all risks are controlled to low or effectively zero.

Additional containment provisions for environmental protection

Assign your final containment level.

Containment level I.	
Are all hazards now controlled by this proposed level of containment?	**Yes**

Final classification of the activity, i.e.Class 1/2/3/4. Is the activity notifiable to HSE?

Class 1

Where the containment and control measures fall between two levels, e.g. where level 1 is appropriate with some control measures from level 2, the classification for the activity is equivalent to the HIGHER containment level. All Class 2,3 and 4 projects are notifiable to the Health and Safety Executive through the Health and Safety Unit

Do you intend to apply <u>all</u> control measures from your highest selected level of containment (See Annex 1)**? If not, please justify the exclusion of any control measures not used.**

Yes

Formal application to the Health and Safety Executive is required for derogation from the full containment level for all Class 2, 3 and 4 projects.

***EC Regulation requires notification of transboundary movements of Class 3 GMMs to the Biological Clearing House and European Commission *(transboundary movements are those entering or leaving the EC)*. If your work involves Class 3 GMMs please indicate below whether they will be subject to transboundary movements.**

Workers Involved in the Project and Facilities Used for the Work

Please indicate the areas where work will be carried out (including Room No. and Designation):	
Room No. and designation	**ACGM Categorisation**
T208b	

Workers initially involved in work:	**Post/experience/training:**
Robert Thomas	Lecturer – 5 years experience of class II cell culture
Training and assessment of competence for existing and future personnel ***Specify arrangements for provision for existing and future personnel***	
Standard laboratory training SOP	

Authorisation and Notification

The work proposed should be discussed with the Departmental Biological Safety Officer.

Signature of proposer ..... Date 4/09/08

Please print name ROB THOMAS

Signature of Biological Safety Officer or authorised Deputy ..... Date 05/07/08

Please print name R I TOMPSETT

NB The Approval of the University's relevant Safety Committee is required before work starts.

APPROVAL of the RELEVANT SAFETY COMMITTEE

On behalf of SC C. M. Nave. Approval Date 17/9/08

ANNEX 1

TABLES OF CONTROL MEASURES AND CONTAINMENT LEVELS

The basic principles of classification are that you:

1. Determine the containment and control measures required by the risk assessment to control the risk of the activity;
2. Where this corresponds to a single containment level this will read across directly to give you the activity class, i.e. level 1 = class 1, level 2 = class 2, etc;
3. Where the measures identified correspond to measures from two different levels of containment the class corresponds to the higher of the two levels.

Further information can be found in the guide to the Contained Use Regulations and in the ACGM Compendium of guidance

***

Please consider the table(s) overleaf. Select the appropriate table for the work you are involved in. In most cases this will be **Table 1A (Laboratory Activities)**. **Where your project involves the use of GMMs in plant growth facilities or animal facilities, you should consider Table 1B or 1C <u>in conjunction</u> with table 1A.** (In the final column of Tables 1B and 1C "additional" specifies use of that control measure in addition to the measures in Table 1A, while "modification" specifies that this measure shall be substituted for the relevant measure in Table 1A).

Large scale activities should be classified using **Table 2.**

Select your control measures. You should place a **X** in the appropriate box on each row to indicate whether that containment measure is required or not.

Determine the corresponding level of containment and hence the class of GMO. Where controls are selected from more than one containment level the Class corresponds to the higher of the containment levels.

FOR FURTHER INFORMATION PLEASE REFER TO ACGM NEWSLETTER 27 OR THE ACGM COMPENDIUM OF GUIDANCE

Please delete tables not relevant to your risk assessment. You may also delete this explanatory page from your final risk assessment

TABLES OF CONTAINMENT MEASURES

TABLE 1A: LABORATORY ACTIVITIES

TABLE 1B: PLANT GROWTH FACILITIES

TABLE 1C: ANIMAL FACILITIES

TABLE 2: OTHER ACTIVITIES (LARGE SCALE)

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TABLE 1A: LABORATORY ACTIVITIES

Containment measures	Containment level 1	Containment level 2	Containment level 3
Laboratory suite - isolation	Not required	Not required	Required
Laboratory - sealable for fumigation	Not required	Not required	Required
Equipment			
Impervious/easy to clean surfaces	Required for bench	Required for bench	Required for bench and floor
Entry to lab via air lock	Not required	Not required	Required where and to the extent the risk assessment shows it is required
Negative pressure relative to the pressure of the immediate surroundings	Not required	Required where and to the extent the risk assessment shows it is required	Required
Extract and input air in laboratory should be HEPA filtered	Not required	Not required	HEPA filters required for extract air
Use of microbiological safety cabinet/enclosure	Not required	Required where and to the extent the risk assessment shows it is required	Required and all procedures with infective materials required to be contained within cabinet/enclosure
Autoclave	Required on site	Required in the building	Required in the laboratory suite
System of work			
Access restricted to authorised personnel only	Not required	Required	Required
Specific measures to control aerosol dissemination	Not required	Required so as to minimise	Required so as to prevent
Shower	Not required	Not required	Required where and to the extent the risk assessment shows it is required
Protective clothing	Suitable protective clothing required	Suitable protective clothing required	Suitable protective clothing required; Footwear required where and to the extent the risk assessment shows it is required
Gloves	Not required	Required where and to the extent the risk assessment shows it is required	Required
Efficient control of disease vectors (eg for rodents and insects) which could disseminate GMMs	Required where and to the extent the risk assessment shows it is required	Required	Required
Specified disinfection procedures in place	Required where and to the extent the risk assessment shows it is required	Required	Required

	Containment level 1		Containment level 2		Containment level 3	
Waste						
Inactivation of GMMs in effluent from handwash sinks and showers and similar effluents	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
Inactivation of GMMs in contaminated material and waste	Required by validated means		Required by validated means		Required by validated means with waste inactivated in lab. suite	
Other measures						
Laboratory to contain own equipment	Not required		Not required		Required, so far as is reasonably practicable	
An observation window or alternative to be present so that occupants of lab can be seen	Required where and to the extent the risk assessment shows it is required		Required where and to the extent the risk assessment shows it is required		Required	
Safe storage/transport of GMMs	Required where and to the extent the risk assessment shows it is required		Required		Required	
Written records of staff training	Not required		Required where and to the extent the risk assessment shows it is required		Required	

HIGHEST LEVEL OF CONTAINMENT SELECTED ABOVE:

CORRESPONDING CLASS OF GMM:

TABLE 1B: PLANT GROWTH FACILITIES

Containment measures	Containment level 1		Containment level 2		Containment level 3		Additional/Modification
Building							
Permanent structure*	Required where and to the extent the risk assessment shows it is required		Required		Required		Modification
Equipment							
Entry via a separated room with two interlocking doors	Not required		Required where and to the extent the risk assessment shows it is required		Required where and to the extent the risk assessment shows it is required		Additional
Control of contaminated run off water	Required where and to the extent the risk assessment shows it is required		Required so as to minimise run off		Required so as to prevent run off		Additional
System of Work							
Effective control of disease vectors such as insects, rodents, arthropods which could disseminate GMMs	Required		Required		Required		Additional
Effective control of pollen, seeds and other plant material which could disseminate GMMs	Required where and to the extent the risk assessment shows it is required		Required so as to minimise dissemination		Required so as to prevent dissemination		Additional
Procedures for the transfer of living material between plant growth facilities, protective structure and laboratory shall control dissemination of GMMs	Required so as to minimise dissemination		Required so as to prevent dissemination		Required so as to prevent dissemination		Additional

*A permanent structure refers to a fixed structure with walls, roof and floor. Where the structure is a greenhouse, that structure shall also have a continuous waterproof covering and self closing, lockable doors, and be located on a site designed to prevent the entry of surface run off water.

TABLE 1C: CONTAINMENT MEASURES FOR ACTIVITIES IN ANIMALS UNITS

Containment measures	Containment level 1	Containment level 2	Containment level 3	Additional/Modification
Facilities				
Isolation of animal unit (Note 1)	Required where and to the extent the risk assessment shows it is required	Required	Required	Modification
Animal facilities(Note 2) separated by lockable doors	Required where and to the extent the risk assessment shows it is required	Required	Required	Additional
Animal facilities (cages etc) designed to facilitate decontamination (waterproof and easily washable material)	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required	Additional
Floor and/or walls and ceiling easily washable	Required where and to the extent the risk assessment shows it is required	Required for floor	Required for floor and walls	Modification
Appropriate filters on isolators or isolated rooms (Note 3)	Not required	Required where and to the extent the risk assessment shows it is required	Required	Additional
Incinerator for disposal of animal carcasses	Required to be accessible	Required to be accessible	Required to be accessible	Additional
Appropriate barriers at the room exit, and at drains or ventilation duct work	Required	Required	Required	Additional
Animals kept in appropriate containment facilities such as cages, pens or tanks but not isolators	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Additional
Animals kept in isolators	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required	Additional

Note 1: In the table, "Animal Unit" means a building or separate area within a building, containing an animals facility and other areas such as changing rooms, showers, autoclaves, food storage areas etc.
Note 2: In the table, "animal facility" means a facility normally used to house stock breeding or experimental animals or one which is used for the performance of minor surgical procedures on animals.
Note 3: "Isolators" means transparent boxes where small animals are contained within or outside a cage; for large animals, isolated rooms may be appropriate.

TABLE 2: CONTAINMENT MEASURES FOR ACTIVITIES INVOLVING LARGE SCALE WORK

Containment measures	Containment level 1	Containment level 2	Containment level 3
General			
Visible micro-organisms should be contained in a system which separates the process from the workplace and wider environment (closed system)	Required where and to the extent the risk assessment shows it is required	Required	Required
Closed systems located within a controlled area	Not required	Required where and to the extent the risk assessment shows it is required	Required
Control of exhaust gases from the closed system	Not required	Required so as to minimise release	Required so as to prevent release
Control of aerosols during sample collection, addition of material to a closed system or transfer of material to another closed system	Required where and to the extent the risk assessment shows it is required	Required so as to minimise release	Required so as to prevent release
Inactivation of bulk culture fluids before removal from the closed system	Required where and to the extent the risk assessment shows it is required	Required by validated means	Required by validated means
Seals should be designed so as to minimise or prevent release	Not required	Required so as to minimise release	Required so as to prevent release
Controlled area designed to contain spillage of the entire contents of the closed system	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required
Controlled area sealable to permit fumigation	Not required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required
Biohazard signs posted	Required where and to the extent the risk assessment shows it is required	Required	Required
Equipment			
Entry via airlock	Not required	Not required	Required where and to the extent the risk assessment shows it is required
Surfaces resistant to water, acids, alkalis, solvents, disinfectants, decontamination agents and easy to clean	Required for any bench	Required for any bench	Required for bench and floor
Specific measures to adequately ventilate the controlled areas in order to minimise air contamination	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required

Containment measures	Containment level 1		Containment level 2		Containment level 3	
Equipment (continued)						
Controlled area maintained at an air pressure negative to the immediate surroundings	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
Extract and input air from the controlled area should be HEPA filtered	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
System of work						
Access restricted to nominated personnel only	Not required		Required		Required	
Decontamination and washing facilities provided for personnel	Required		Required		Required	
Personnel should shower before leaving the controlled area	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
Personnel should wear protective clothing	Work clothing required		Work clothing required		Required	
Written procedures and records of staff training	Not required		Not required		Required	
Waste						
Inactivation of GMMs in contaminated material and waste including those in process effluent before final discharge	Required by validated means		Required by validated means		Required by validated means	
Inactivation of GMMs in effluent from handwashing sinks and showers or similar effluents	Not required		Not required		Required where and to the extent the risk assessment shows it is required	

HIGHEST LEVEL OF CONTAINMENT SELECTED:

CLASS OF GMM:

ReNeuron

ReNeuron Project Number: GM08/001

CONFIDENTIAL

PROPOSAL AND RISK ASSESSMENT FOR GENETICALLY MODIFIED ORGANISMS

Title of Project: Culture, handling and storage of CTX0E03, a regulated c-MycER^{TAM} human cell line.

Project Supervisor: K. Pollock

Date of Review: 19 May 2008

Location of Work: ReNeuron Laboratories

ReNeuron Project Number: GM08/001

PART ONE - Personnel

Briefly indicate your experience of working with microorganisms and genetically manipulated organisms and any training you have received
Kenneth Pollock, BSc PhD 20yrs tissue culture; PhD; Post Doc , Senior scientist Aventis (RPR) 2 yrs bacterial culture >10 yrs work with GMM's

Other workers on the project [if known]	Qualifications	Experience/Training
Erik Miljan	BSc, PhD	12 years with GMMs
Paul Stroemer	BSc, PhD	10 years with GMMs
Sara Patel	BSc, MSc, PhD	13 years with GMMs
Personnel experienced in genetic modification procedures as authorised by company Heads of Departments		

ReNeuron Project Number: GM08/001

PART TWO

(a) Scientific goals of project

Storage, culture, formulation, transportation and injection of CTX0E03, a regulated c-MycER^{TAM} human cell line

(b) An overview of the different types of GMMs that will be constructed

No GMMs will be constructed in this project.

(i) List of recipient strain(s)

Not applicable.

(ii) list of vector(s)

Not applicable.

(iii) List of function of inserted gene(s)

Not applicable.

(c) An indication of the most hazardous GMM

CTX0E03, a regulated c-MycER^{TAM} human cell line.

(d) Are you confident that for all of the GMMs covered by this assessment there are no harmful properties associated with the recipient strain, the vector, or the inserted material?

Not applicable.

(e) Are you confident that none of the final GMMs could be hazardous to humans or the environment?

Yes.
See Part Three of this proposal

PART THREE

A. c-myc transgenes

(a) **Hazards to human health**

(i) Hazards associated with the recipient microorganism (e.g. bacterial host or viral vector)

Not applicable

(ii) Hazards arising directly from the inserted gene product (e.g. cloning of a toxin gene or oncogene)

Not applicable

(iii) Hazards arising from the alteration of existing traits (e.g. alteration of pathogenicity, host range, tissue tropism, mode of transmission or host immune response)

The GMO is created from the introduction of a conditional immortalizing gene
Used to enhance the growth properties of cells *in vitro*. The hazards arising from the alteration of existing traits is effectively zero. Please refer to GMO Risk Assessment GM07/002 for full details.

(iv) The potential hazards of sequences within the GMM being transferred to related microorganisms

The hazards are that any infected related micro-organisms would express the c-mycER protein and may possibly become immortalized or oncogenic. The risk of this happening is low. In addition the regulated c-myc transgene requires exogenous 4-hydroxytamoxifen for fully functional c-mycER. The likelihood of this happening, other than by design, is effectively zero. Studies to demonstrate the stability (genomic insertion and sequence) of the transgene and the lack of replication competent retroviruses have been employed and are summarized below.

(b) **Assignment of a provisional containment level that is adequate to protect against hazards to human health**

Hazards may be derived from source material (human tissue) and genetic modification as described in GMO Risk Assessment GM07/002. The associated hazards of the GMMs used in this project may be classified in Hazard Group 1, as it is unlikely that CTX0E03 cells will cause human disease. Work involving bulk culture of cells where the cells are open to the environment can be performed at Containment level 1.

The rationale for classifying CTX0E03 cells as Hazard Group 1 in regards to hazards to human health is as follows:

-CTX0E03 cells have been tested for the stability of the c-mycER^{TAM} transgene by PCR to assess the integration site and sequence and the transgene has been found to be stable (BioReliance reports 1053643.106602 and 1053643.106631).

-CTX0E03 cells have been screened for the presence of viral contaminants, and no evidence was obtained in an *in vivo* assay using embryonated eggs, suckling mice, adult mice and guinea pigs (BioReliance report 1053643.37027)

-CTX0E03 cells have been screened for the presence of viral contaminants, and no evidence was obtained in an *in vitro* assay using 3 detector cell lines (BioReliance report 1053643.003000)

-Replication competent retroviruses are not detected in CTX0E03 (BioReliance report 1053643.011624)

-CTX0E03 cells have been screened for the presence of bovine viral contaminants and cytopathic effects, haemadsorption and specific immunofluorescence were not observed (BioReliance report 1053643.032930)

-CTX0E03 cells have been screened for the presence of porcine viral contaminants and no viral contaminants were found (BioReliance report 1053643.033900)

-CTX0E03 cells have been screened for the presence of murine viral contaminants and no viral contaminants were found (BioReliance report 1053643.37001)

-CTX0E03 cells have been screened for the presence of Parvovirus B19 and were found to be negative (BioReliance report 1053643.107016)

-CTX0E03 cells have been tested for the detection of viruses, virus-like particles, fungi, yeasts, bacteria and mycoplasmas and were found to be negative (BioReliance report 1053643.013013)

-CTX0E03 cells have been tested for the presence of retroviral reverse transcriptase activity and were found to be negative (BioReliance report 1053643.37405)

-CTX0E03 cells have been screened for a variety of human viruses (HCV, HBV, HIV-I, HIV-II, HTLV, HHV-8, HHV-7, HHV-6, EBV, hCMV and SV40) and were found to be negative (BioReliance report 1053643.107069)

-CTX0E03 cells have been tested for tumour formation in athymic mice and no evidence of tumour formation was found (BioReliance report 05PJ55.37138)

(c) Identification of any hazards to the environment

(i) Hazards associated with the recipient microorganism (e.g. bacterial host or viral vector)

Not applicable

(ii) Hazards arising directly from the inserted gene product

It is unlikely that the inserted gene product would pose a serious risk to animals or plants in the environment because the gene product/protein cannot be transferred to another host.

(iii) Hazards arising from the alteration of existing traits (e.g. alteration of pathogenicity, host range or tissue tropism)

Not applicable

(iv) The potential hazards of sequences within the GMM being transferred to related microorganisms

Transduced human cells. The hazards are that any infected related micro-organisms could become infected and may possibly become immortalized or oncogenic. The risk of this happening is low. In the event of a breach of containment the likelihood that human cells may survive and 'infect' other micro-organisms is low.

It is unlikely that transfer of sequences from the GMM to other related micro-organisms would pose a serious risk to animals or plants in the environment.

(d) **Consideration of the nature of the work to be undertaken and a detailed review of the control measures**

(i) **Are any of the work procedures likely to generate aerosols?**
There is a risk of aerosol generation during centrifugation steps. All work carried out in sealed rotors.

There is a risk of aerosol generation if grafting syringes are emptied in air. This risk will be controlled by emptying grafting syringes in liquid as described in local rules.

(ii) **How will waste materials be disposed of?**

Any disposable materials used will be soaked in not less than 1% Virkon or Trigene overnight then incinerated as clinical waste. Waste liquids will be diluted in excess Virkon or Trigene (final concentration >1%) overnight then disposed down waste drains.

Syringes used in grafting will be flushed in 70% alcohol containing hibitane.

(iii) **Will it be necessary to use sharps?**
Yes during implantation procedures in pre-clinical studies

(iv) **If the work involves the experimental infection of animals is it known whether the animal will shed the GMM?**
It is not known if animals shed the GMM.. Following implantation in brain the incidence of cells in peripheral tissues is extremely low .

(v) **If the work involves the experimental infection of plants what is known about the likely route of transmission of the GMM?**
Not applicable

(vi) **In the case of organisms whose multiplication involves a complex life-cycle will the work involve the propagation of organisms that are in stages in that life-cycle that are particularly hazardous?**
Not applicable

(vii) **Have any disinfectants been validated under the actual conditions of use?**
No. Refer to attached manufacturers validation data.

(viii) **Does the nature of this work preclude it being undertaken by any workers who have a serious skin condition (e.g. eczema) or other health problems that might make them more susceptible to infection (e.g. some kind of immunological defect)?**
Yes. Any persons with exposed or open wounds or lesions will not be allowed to perform the activities where live cells are involved. Appropriate PPE is used in all circumstances.

(ix) **Will workers receive any vaccinations or health surveillance?**
Yes. All workers handling this material must have been vaccinated against hepatitis B.

(e) **Consideration of whether there is a need to assign additional measures over and above the provisional level of containment.**
None

(f) **Does your Department safety plan provide adequate protection and provision for an emergency action in case of accidental release?**
Yes. A documented spillage procedure exists for actions in case of accidental release.

PART FOUR:

This project has been assigned as a Class 1 activity for which containment level 1 is appropriate to protect human health and the environment.

ReNeuron Project Number: GM08/001

PART FIVE - Signatures

Signed: .....
(Project Supervisor/proposer)

Date: 19 May 2008

Signed: .....
(Head of Department)

Date: 19 May 2008

Approval for the project

Signed: .....
(Biological Safety Officer/Deputy)

Date: 19 May 2008

Signed: .....

Date: 19th May 2008

(Chair/Vice-Chair of GMSC)

ReNeuron Project Number: GM08/001