Annual Review of Risk Assessment Made Under:
Genetically Modified Organisms (Contained Use) Regulations 2014

Department: Nuffield Division of Clinical Laboratory Sciences
Radcliffe Department of Medicine

Supervisor: Prof Stephen Hyde

Ref No: CBGM01

Title: Expression of human and other mammalian genes encoding the multidrug resistance, cystic fibrosis proteins and viral proteins in baculovirus insect cell systems and mammalian cells

The Risk Assessment has been reviewed: YES
Key aspects: identification of any potentially harmful effects, characteristics of the proposed activity, the severity of any potentially harmful effects, the likelihood of them occurring and disposal of waste and effluent.

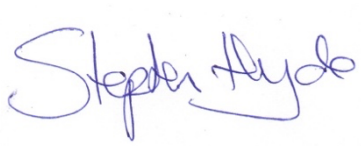
List any additional transgenic sequences: None

Appropriate containment measures have been confirmed: YES
Complete attached containment levels/measures table

Original containment level and risk classification remain valid: YES

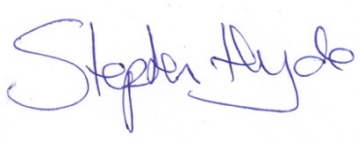
Classification and assignment of final control measures:
Containment Level: CL1
Risk Classification: 1

Reviewed By:
Date (YYYY-MM-DD):



Prof Stephen Hyde
2024-08-16

Approved By Genetic Modification Safety Committee
Agreed By One-Of DSO/BSO/HoD:
Date (YYYY-MM-DD):



Prof Stephen Hyde – NDCLS BSO
2024-10-02

Approved by Head of Department
Date (YYYY-MM-DD):

Prof Deborah Gill – NDCLS HoD
2024-10-02

Next Review Due:
Before end 2025

List Of Associated Transgenic Sequences:

Common Reporter Genes:
EGFP and similar proteins
Luciferase and similar proteins
Beta-galactosidase and similar proteins
Chloramphenicol acetyl transferase and similar proteins

Bacterial Proteins
Salmonella typhimurium oligopeptide permease oppABCD and similar ABC proteins

Mammalian ion channels/transporters proteins:
Cystic fibrosis transmembrane conductance regulator (CFTR),
Multi-drug resistance p-glycoprotein (MDR, PGP)

Risk Assessment Users & Supervisor During Previous Year

Stephen Hyde

Table 1a Containment measures applicable to contained use involving micro-organisms in laboratories

Containment Measures		**Containment Levels**			
		CL1	CL2	CL3	CL4
Facilities					
1	Laboratory suite: isolation[1]	not required	not required	required	required
2	Laboratory: sealable for fumigation	not required	not required	required	required
Equipment					
3	Surfaces impervious to water, resistant to acids, alkalis, solvents, disinfectants and decontamination agents and easy to clean	required for any bench	required for any bench	required for any bench and floor	required for any bench, floor, ceilings and walls
4	Entry to laboratory via airlock[2]	not required	not required	required where and to extent the risk assessment shows it is required	required
5	Negative pressure relative to the pressure of the immediate surroundings	not required	not required	required except for activities where transmission does not occur by the airborne route	required
6	Extract and input air from the laboratory must be HEPA filtered	not required	not required	HEPA filters required for extract air except for activities where transmission does not occur by the airborne route	HEPA filters required for input and extract air[3]
7	Microbiological safety cabinet/ enclosure	not required	required where and to extent the risk assessment shows it is required	all procedures with infective materials required to be contained within a cabinet/ enclosure	required, and all procedures with infective materials required to be contained within a cabinet/ enclosure
8	Autoclave	required on site	required in the building	required in the laboratory suite[4]	double ended autoclave required in laboratory

Containment Measures		Containment Levels			
		CL1	~~CL2~~	~~CL3~~	~~CL4~~
System Of Work					
9	Access restricted to authorised personnel only	not required	~~required~~	~~required~~	~~required (via airlock key procedure)~~
10	Biohazard sign on door	not required	~~required~~	~~required~~	~~required~~
11	Specific measures to control aerosol dissemination	not required	~~required so as to minimise~~	~~required so as to prevent~~	~~required so as to prevent~~
12	Shower	not required	~~not required~~	~~required where and to extent the risk assessment shows it is required~~	~~required~~
13	Protective clothing	suitable protective clothing required	~~suitable protective clothing required~~	~~suitable protective clothing required; footwear required where and to extent the risk assessment shows it is required~~	~~complete change of clothing and footwear required before entry and exit~~
14	Gloves	not required	~~required where and to extent the risk assessment shows they are required~~	~~required~~	~~required~~
15	Efficient control of disease vectors (eg rodents and insects) which could disseminate GMMs	required where and to extent the risk assessment shows it is required	~~required~~	~~required~~	~~required~~
Waste					
16	Inactivation of GMMs in effluent from hand- washing sinks and showers and similar effluents	not required	~~not required~~	~~required where and to extent the risk assessment shows it is required~~	~~required~~
17	Inactivation of GMMs in contaminated material and waste	required by validated means where and to extent the risk assessment shows it is required	~~required by validated means~~	~~required by validated means, with waste inactivated within the laboratory suite~~	~~required by validated means, with waste inactivated within the laboratory~~

Containment Measures		Containment Levels			
		CL1	~~CL2~~	~~CL3~~	~~CL4~~
Other Measures					
18	Laboratory to contain its own equipment	not required	~~not required~~	~~required, so far as is reasonably practicable~~	~~required~~
19	An observation window or alternative is to be present so that occupants can be seen	required where and to extent the risk assessment shows it is required	~~required where and to extent the risk assessment shows it is required~~	~~required where and to extent the risk assessment shows it is required~~	~~required~~
20	Safe storage of GMMs	required where and to extent the risk assessment shows it is required	~~required~~	~~required~~	~~secure storage required~~
21	Written records of staff training	not required	~~required where and to extent the risk assessment shows it is required~~	~~required~~	~~required~~

1 “isolation” means, in relation to a laboratory, separation of the laboratory from other areas in the same building, or being in a separate building.

2 Entry must be through an airlock which is a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities and preferably by interlocking doors.

3 Where viruses are not retained by the HEPA filters, extra requirements will be necessary for extract air.

4 Where the autoclave is outside the laboratory in which the contained use is being undertaken, but within the laboratory suite, there must be validated procedures for the safe transfer of material into that autoclave, which provide a level of protection equivalent to that which would be achieved by having an autoclave in that laboratory.

Table 1b Containment measures applicable to contained use involving micro-organisms in plant growth facilities (to be read with Table 1a)

Omitted as not relevant to NDCLS activities

Table 1c Containment measures applicable to contained use involving micro-organisms in animal units (to be read with Table 1a)

Omitted as not relevant to NDCLS activities

Containment Measures		Containment Levels				Additional / Modification
		CL1	CL2	CL3	CL4	
Facilities						
1	Isolation of animal unit[1]	required where and to extent the risk assessment shows it is required	required	required	required	modification
2	Animal facilities[2] separated by lockable doors	required where and to extent the risk assessment shows it is required	required	required	required	additional
3	Animal facilities (cages, etc) designed to facilitate decontamination (waterproof and easily washable material)	required where and to extent the risk assessment shows it is required	required where and to extent the risk assessment shows it is required	required	required	additional
4	Floor, walls and ceiling easily washable	required where and to extent the risk assessment shows it is required	required for floor	required for floor and walls	required for floor, walls and ceiling	Modification
5	Appropriate filters on isolators or isolated rooms[3]	not required	required where and to extent the risk assessment shows it is required	required	required	additional
6	Appropriate barriers at the room exit, and at drains or ventilation duct work	required	required	required	required	additional
7	Animals kept in appropriate containment facilities, such as cages, pens or tanks but not isolators	required where and to extent the risk assessment shows it is required	required where and to extent the risk assessment shows it is required	required where and to extent the risk assessme nt shows it is required	required where and to extent the risk assessment shows it is required	Additional
8	Animals kept in isolators	not required	required where and to extent the risk assessment shows it is required	required	required	modification

1 "animal unit" means a building, or separate area within a building, containing an animal facility and other areas including changing rooms, showers, autoclaves and food storage areas.

2 "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.

3 "isolators" means transparent boxes where small animals are contained within or outside a cage; for large animals, isolated rooms may be more appropriate

Review of risk assessment under the transitional arrangements of the Genetically Modified Organisms (Contained Use) Regulations 2000

Department: NDCLS

Supervisor: Dr SC HYDE

Ref. No: CB GM1

Project Title: EXPRESSION OF HUMAN AND OTHER Mammalian genes encoding the multidrug resistance, cystic fibrosis protein and viral proteins in baculovirus/insect cell systems and mammalian cells

✓ The above risk assessment has been reviewed

✓ Appropriate containment measures have been selected as indicated on the attached table(s) and

either

✓ (i) the original risk assessment remains valid

or

... (ii) the following changes have been made to the risk assessment

ENVIRONMENTAL RISK ASSESMENT RE EVALUATED.

Classification and assignment of final control measures

In the following complete the centre section in response to prompts in left column using guidance in right column

Classification		*GUIDANCE*
	Class I	*The highest numbered column in which a control measure is required indicates the Class of the activity - circle class on table 1a*
Assign corresponding level of containment	**Containment Level** I	*The class number indicates the minimum containment level required*
specify which, if any, of the optional control measures at this containment level are required	NA	*The optional control measures are listed on the table as "may be required"*
specify any other control measures required	NA	

Reviewed By:

Signature: Stephen Hyde Date: 27/1/2000

Review approved by Genetic Modification Safety Committee **Yes/No**

Signature: Date:

(Biological Safety Officer)

CBGM1

RISK ASSESSMENT

Made under the

GENETICALLY MODIFIED ORGANISMS (CONTAINED USE) REGULATIONS 1992

DEPARTMENT: Nuffield Dept. of Clinical Biochemistry

SUPERVISOR: Prof. C.F. Hobbs Dr S.C. Hyde 1/1/98 Stephen

TITLE OF PROJECT: Expression of human and other mammalian genes, encoding the multidrug resistance and cystic fibrosis proteins and integrases, in baculovirus/insect cell systems and mammalian cells SH 1/97 CFH 11/95

Description: optimisation of translation, mutation of open reading frames see also CBGM4.

Assessed By: C.F. Hobbs

Signature: C. Hyde **Date:** 10/1/95

RISK ASSESSMENT APPROVED BY GENETIC MODIFICATION SAFETY COMMITTEE: (YES/NO)

Signature : S/H Abbott **Date:** 8/2/95

PERMISSION GRANTED BY HEAD OF DEPARTMENT FOR PROJECT TO BE UNDERTAKEN: (YES/NO)

Signature : C. Hyde **Date:** 12/1/95

CHARACTERISTICS OF, AND HANDLING PRECAUTIONS FOR, RECIPIENT (HOST) AND DONOR ORGANISMS

	RECIPIENT	DONOR
What is the full name of the organism? (Include species, subspecies and strain as appropriate.)	Insect cells (several species) Mammalian cells CHO	Mammalian Species
Is the organism wild type or disabled? [see Appendix 1 for list of known disabled organisms]	~~WILD TYPE~~ / (DISABLED)	(WILD TYPE) / ~~DISABLED~~
Is the organism pathogenic for man?	YES / (NO)	YES / (NO)
ACDP Hazard Group of organism:	(1) / 2 / 3 / 4	(1) / 2 / 3 / 4
Are there any other hazards of the organism or its products? If yes identify type: - toxic, allergenic, oncogenic, carcinogenic, other (specify)	YES / (NO)	YES / (NO)
Is the organism pathogenic for plants or animals?	YES / (NO)	YES / (NO)
Control measures: - Containment Level	(1) / 2 / 3 / 4	(1) / 2 / 3 / 4
- additional precautions (circle)	microbiological safety cabinet gloves avoid use of sharps other (specify)	microbiological safety cabinet gloves avoid use of sharps other (specify)

DESCRIPTION OF THE GENETIC MODIFICATION

Technique used to introduce the vector or insert into the organism:	Lipofection, Infection or electroporation
Nature and source of the vector:	Baculovirus derivatives E-coli plasmids CHO
Function of the genetic modification and/or of the new nucleic acid:	Protein production

Polyhedrin Negative

FOR GENETICALLY MODIFIED BACTERIA:

ASSESSMENT OF RISK TO HUMAN HEALTH AND ASSIGNMENT OF CONTAINMENT/CONTROL MEASURES

ASSIGNMENT TO CONTAINMENT:
[see Appendix 2 for guidance in assigning values]

Overall Value: 10^{-12} (Access) x 1 (Expression) x 10^{-9} (Damage) = 10^{-21}

CIRCLE OVERALL VALUE AND CORRESPONDING ACGM CONTAINMENT LEVEL BELOW

Overall Value:	(10^{-15} or lower)	10^{-12}	10^{-9}	greater than 10^{-9}
Containment Level:	(1)	2	3	*contact Safety Office

HEALTH CONSIDERATIONS:

How does the pathogenicity of the GMO compare to that of the donor and recipient

GMO (less) / equivalent / more pathogenic than donor
GMO (less) / equivalent / more pathogenic than recipient

Are there any other hazards of the GMO or its products? If yes identify: - toxic, allergenic, oncogenic, carcinogenic, other (specify)	YES / (NO)
Are any additional precautions necessary? If yes circle as appropriate:	YES / (NO) microbiological safety cabinet gloves avoid use of sharps other (specify)
After consideration of the actual procedures to be undertaken are the control measures assigned to protect human health adequate? If no specify what additional measures are needed:	(YES) / NO

FOR GENETICALLY MODIFIED VIRUSES (TO INCLUDE VIRAL VECTORS):

ASSESSMENT OF RISK TO HUMAN HEALTH AND ASSIGNMENT OF CONTAINMENT/CONTROL MEASURES	
What is the natural host range of the virus?	INSECTS
Is there reason to suspect that the modified virus may have altered interaction with host defence mechanisms? If yes specify how:	YES / (NO)
Is there reason to suspect that the tissue tropism or the host range of the recombinant virus will be different from that of the modified virus? If yes specify likely alteration:	YES / (NO)
Will viral susceptibility to antiviral drugs (where these are available) or other control agents be affected by genetic modification? If yes specify:	YES / (NO)
Does the insert code for protein(s) with known or suspected pharmacological or physiological effect? If yes specify:	YES / (NO)
Is the insertion likely to result in any other harmful effects? If yes specify:	YES / (NO)
If the virus is disabled what is the possibility of reversion such that any disablement is overcome?	HIGH / MEDIUM (LOW)
Has the replication competence of the viral vector been confirmed? Both: - prior to modification - following modification	 (YES) / NO (YES) / NO
How does the pathogenicity of the GMO compare to that of the donor and recipient GMO (less) / equivalent / more pathogenic than donor GMO (less) / equivalent / more pathogenic than recipient	
Are there likely to be any other hazards associated with the replication or integration of the GMO into a host cell? If yes identify: - toxic, allergenic, oncogenic, carcinogenic, other (specify)	YES / (NO) Non mammalian promoter sequences
The control measures indicated on the basis of the assessment of risk to human health are: - Containment Level - additional precautions (circle)	 (1) / 2 / 3 / 4 microbiological safety cabinet gloves avoid use of sharps other (specify)

RISK ASSESSMENT FOR ENVIRONMENTAL PROTECTION

Do any of the following characteristics of the GMO result in a potential hazard to the environment	Cell Lines	Baculovirus
- capacity to survive, establish, disseminate and/or displace other organisms	YES / (NO)	NO
- pathogenicity to animals or plants	YES / (NO)	NO
- potential for transfer of genetic material between the GMO and other organisms	YES / (NO)	YES
- products of gene expression particularly of they are toxic)	YES / (NO)	NO
- other negative effects on organisms	YES / (NO)	NO
- phenotypic and genetic stability	YES / (NO)	NO
If NO hazards identified circle:	NO ENVIRONMENTAL HAZARDS IDENTIFIED - NO ADDITIONAL PRECAUTIONS NECESSARY for cell line	

If hazards are identified then estimate:

for Baculovirus

LIKELIHOOD OF HAZARD(S) being manifested (taking containment into account): HIGH/ MEDIUM / LOW / (NEGLIGIBLE)

CONSEQUENCES OF HAZARDS being manifested: SEVERE / MEDIUM / LOW / (NEGLIGIBLE)

CIRCLE RISK IN MATRIX AS APPROPRIATE:

CONSEQUENCE OF HAZARD	LIKELIHOOD OF HAZARD: High	Medium	Low	Negligible
Severe	High	High	Medium	Effectively Zero
Medium	High	Medium	Medium/ Low	Effectively Zero
Low	Medium/ Low	Low	Low	Effectively Zero
Negligible	Effectively Zero	Effectively Zero	Effectively Zero	Effectively Zero

If risks are low or effectively zero circle:	NO ADDITIONAL PRECAUTIONS NECESSARY TO PROTECT ENVIRONMENT OTHER THAN THOSE TO PROTECT HUMAN HEALTH for Baculovirus.
Otherwise specify additional control measures to reduce all risks to low/effectively zero:	

CLASSIFICATION OF THE GENETICALLY MODIFIED ORGANISM	
Is the final GMO pathogenic? For:	Cell Line + Baculovirus.
- humans	YES / (NO)
- animals	YES / (NO)
- plants	YES / (NO)
Does the insert code for any potentially pathogenic or harmful traits that will result in a pathogenic or harmful phenotype (to man or the environment) of the GMO?	YES / (NO)
Have any antibiotic resistance markers been introduced which could compromise the treatment of any infection that may occur?	YES / (NO)
If the answer to any of the above is YES circle:	Group 2
If all NO then:	
Does the genetically modified micro-organism meet the criteria for classification as Group 1 [see Appendix 3 for guidance]	(YES) / NO
If YES circle:	(Group 1)
If NO circle:	Group 2

CLASSIFICATION OF ACTIVITY	
TEST OF PURPOSE: Is the activity being undertaken for any one or more of the following purposes? - teaching, research, development, nonindustrial, non-commercial	(YES) / NO
TEST OF SCALE: Is the activity "small scale" ie. is the culture contained and easily inactivated using standard laboratory techniques?	(YES) / NO
If the answer to both of the above questions is yes circle: If answer to either is no circle:	(Type A) Type B

Table 1a: Containment Measures for Activities involving GMMs in Laboratories

Where a item is listed as "may be required" this indicates the item to be an option at that particular containment level and its requirement should be determined by the risk assessment for the particular activity concerned. Delete no or yes as indicated by risk assessment.

Containment Measures	Containment Levels			
	1	2	3	4
Isolated laboratory suite	not required	not required	required	required
Laboratory sealable for fumigation	not required	not required	required	required
Surfaces impervious, resistant and easy to clean	required for bench	required for bench	required for bench and floor	required for bench, floor, ceiling and walls
Entry to lab via airlock	not required	not required	may be required no / yes	required
Negative pressure relative to the pressure of the immediate surroundings	not required	may be required no / yes	required	required
HEPA filtered extract and input air	not required	not required	required for extract	required for input and extract
Microbiological safety cabinet/enclosure	not required	may be required no / yes	required	required (class 3)
Autoclave	required on site	required in the building	required in the lab suite	required in lab (double ended)
Access restricted to authorised personnel	not required	required	required	required
Specified measures to control aerosol dissemination	not required	required so as to minimise	required so as to prevent	required so as to prevent
Shower	not required	not required	may be required no / yes	required
Protective clothing	suitable protective clothing required	suitable protective clothing required	suitable protective clothing required	complete change of clothing and footwear
Gloves	not required	may be required no / yes	required	required
Control of disease vectors (eg rodents, insects) which could disseminate GMMs	may be required no / yes	required	required	required
Specified disinfection procedures in place	may be required no / yes	required	required	required
Inactivation of GMMs in effluent from handwashing sinks, showers etc	not required	not required	may be required no / yes	required
Inactivation of GMMs in contaminated material and waste	required by validated means	required by validated means	required by validated means	required by validated means
Laboratory to contain its own equipment	not required	not required	required	required
An observation window or alternative so that occupants can be seen	may be required no / yes	may be required no / yes	required	required
Safe storage of GMMs	may be required no / yes	required	required	secure storage required
Written records of staff training	not required	may be required no / yes	required	required

CLASSIFICATION	CLASS 1	CLASS 2	CLASS 3	CLASS 4