



agriculture, forestry & fisheries

Department:
Agriculture, Forestry and Fisheries
REPUBLIC OF SOUTH AFRICA

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APPLICATION TO REGISTER A FACILITY FOR ACTIVITIES INVOLVING GENETIC MODIFICATION

- Please consult the Standard Operating Procedures relevant for Regulation 2(2) and Regulation 4 prior to completing this form.
- Please answer all relevant sections of the form CLEARLY in accordance with the Guidelines in terms of the GMO Act, and any other applicable legislation, with particular reference to the Occupational Health and Safety Act, 1993 (Act No. 85 of 1993).
- Please return your completed application to the Registrar at the address given above. Your application must consist of the following components –
 - Proof of payment of the correct fee
 - Map indicating the position of the facility as well as each unit within the facility
 - Map indicating floor plan/laboratory layout
 - A list containing the following information – all the units involved, the responsible person for each unit and the proposed activity in each unit
 - Risk assessment according to prescribed format (see below) for each project within the facility.
 - Original CBI application – This application is referred to as the Confidential Business Information (CBI) application and contains information that you may regard as confidential information.
 - One complete copy of the original CBI application
 - **One copy of the non-confidential business information copy (NON-CBI copy) - this is your application where you have deleted any information that you regard as confidential business information. Please take note that you must make reference to the specific section of the Promotion of Access to Information Act, 2000 whenever you “delete” information in this application.**
 - One electronic copy i.e. CD of the non-CBI application and risk assessment

☐	☐	☐	☐
New	Amendment	Rescinded	Renewal

(Indicate the previous registration number)

PART I

Section 1

1A Details of facility where the work is to be carried out

(University, Institute or Company etc. carrying out the work)

- Name of the Organisation
- Department
- Address

1B Details of person responsible for the work

(i.e. person authorised by University, Institute or Company as the person managerially responsible for all activities involving genetic modification to be undertaken at the facility. This will often be a Head of Section, Research Manager, or similar. They are not necessarily involved in genetic modification themselves).

- Title
- Initials
- Surname
- Position
- Telephone No
- Facsimile No
- Mobile
- E-mail
- Qualifications
- Other relevant training

2 Brief description of the facility

(i) (Please tick all relevant boxes to indicate availability)

☐	Laboratory	☐ CL1	☐ CL2	☐ CL3	☐ CL4
☐	Animal containment	☐ CL1	☐ CL2	☐ CL3	☐ CL4
☐	Growth rooms	☐ CL1	☐ CL2	☐ CL3	☐ CL4
☐	Glass house	☐ CL1	☐ CL2	☐ CL3	☐ CL4
☐	Pilot Plant / Production	☐ CL1	☐ CL2	☐ CL3	☐ CL4
Other (please specify):					
.....					
.....					
		☐ CL1	☐ CL2	☐ CL3	☐ CL4

* CL = Containment levels 1 to 4

(ii) Please submit a list of the physical as well as operation characteristics of your facility, and how this supports activities at a certain containment level.

3 Information about waste management

- (i) Provide details of waste treatment including types of waste, quantities, potential hazards and levels of live genetically modified micro-organisms in the waste
- (ii) Information on the waste management techniques used, including recovery of liquid or solid waste and the inactivation techniques used
- (iii) Information on the ultimate form and destination of inactivated waste

4 Information about accident prevention and emergency response plans

- (i) Information on the selection and training of laboratory staff and supervision of work
- (ii) Information on the source of hazards and conditions under which accidents might occur
- (iii) Information on the preventive measures applied such as safety equipment, alarm systems, containment methods and procedures and available resources
- (iv) A description of information given to workers
- (v) A summary of the emergency plan prepared prior to commencement of the activity
- (vi) Information on the policy of disinfection and procedures for the disposal of potentially infective material

- (vii) Provide guidelines for ancillary and maintenance staff, contractors and visitors
- (viii) Information on the maintenance and test procedures of ventilation systems, high efficacy particulate air (HEPA) filters, microbiological safety cabinets and other safety equipment
- (ix) Information on health surveillance which should, where appropriate, include screening procedures including the immune status of the individual, sickness investigation, issue of medical contact cards, immunisation procedures, maintenance of baseline serum samples for staff
- (x) Information on the duties of the biological safety officer

5. Provisions of the Occupational Health and Safety Act, 1993

- (i) What are the implications of the proposed activity with regard to the health and safety of the workers, cleaning personnel and any other person that will be directly or indirectly involved in the activity? Please take into consideration the provisions of the Occupational Health and Safety Act, 1993 (Act No. 181 of 1993) and accompanied regulations.
- (ii) Indicate the proposed health and safety measures that would be applied to safeguard employees during the proposed activity.

6. Risk assessment

- Each project must be accompanied by a separate risk assessment.
- This is currently the suggested format that should be used in terms of a risk assessment, however, you may add to this format to include other/additional information with regard to your project.
- For guidance in conducting the risk assessment, please refer to Guidelines for use by the applicant (available from the website of the Department at www.nda.agric.za) and the provisions of the Occupational Health and Safety Act, 1993 and all accompanied Regulations (available from the Department of Labour)

Program Title: **1.** (Insert the title of the project)

Name of responsible person / people:

Divide the work with Genetically Manipulated Microorganisms (GMMs) in this project into a minimal number of procedures with related risks. Assess each procedure using this form (GMM1) to classify the procedure into Class 1, 2, 3 or 4 as defined by the ACGM (3A).

The process involves assessing each procedure as follows:

- * *Identification of **hazards** to human/animal or the environment, resulting from the recipient, insert, vector and final GMO*
 - * **Consideration of relevant classification schemes (ACDP Hazard Group), giving provisional classification.**
- * *Identification of **risk** (in terms of consequence and likelihood)*
- * *Assign final classification to ACGM Class 1, 2, 3 or 4.*

1. Description of procedure:

2. Recipient Microorganisms

*List **all** recipient microorganisms and ACDP Hazard Group including bacteria (e.g. E. coli strains) viruses (e.g. vaccinia), eukaryotic cell lines (e.g. COS cells, PC12 cells):*

3. Inserted Genes

Give details of all genes or classes of genes (with the organism of origin) to be manipulated:

4. Cloning Vectors

Give details of cloning vectors used.

For example:

- * *Eukaryotic viral vectors*
- * *Plasmid vectors:*

5. Final GMM

Give details of all final GMMs created during the procedure.

6. HAZARD IDENTIFICATION

Identify any hazards to humans or the environment (animals and plants) resulting from the recipient, insert, vector and final GMM. Explain how you reach your conclusions.

- (i) **Consider the properties of the recipient microorganism** (e.g. bacterial host or viral vector).

For example:

- * *Is it listed in Advisory Committee on Dangerous Pathogens (ACDP) hazard groups 2, 3 or 4? Which animals can be infected by the recipient micro-organism? Does it infect domestic or wild animals?*
- * *If it is a disabled micro-organism, is there any possibility of complementation or reversion of the disabling mutations?*

- (ii) **Consider whether the product of the inserted gene has a biological activity, which can act directly to cause harmful effects.**

For example:

- * *Does the inserted DNA encode a toxin, an oncogenic protein, an allergen, a modulator of growth or differentiation (hormone or cytokine) or any other protein with a potentially harmful biological activity?*
- * *When constructing a cDNA or genomic library, consider the properties of the donor organism – might certain clones encode toxins or oncogenes?*
- * *What is the known or suspected biological activity and the levels and nature of the product required to elicit this activity, e.g., activity, toxicity, allergenic or pathogenic effects? The full biological activity may be dependent on posttranslational modification, glycosylation or renaturation, which may, in some cases, only be achieved in certain host organisms. Is the protein to be synthesised as an inactive or active fusion?*

- (iii) **Consider whether the inserted gene encodes a product that might act alongside the existing characteristics of the recipient microorganism, so as to endow the GMM with altered pathogenic properties.**

For example:

- * *Does the inserted gene encode a pathogenicity determinant, such as an adhesin, a penetration factor or a surface component providing resistance to host defence mechanisms?*
- * *Is it possible that expression of the inserted gene could alter the tissue tropism, host range or infectivity as compared to the recipient microorganism?*
- * *Does the inserted DNA encode resistance to an antibiotic other than the commonly used selection antibiotics that might be used for the treatment of a laboratory-acquired infection?*

- (iv) **Consider whether an inserted sequence, that does not give rise to a harmful phenotype in the recipient microorganism, could give rise to harm as a result of natural gene transfer to another, possibly related, organism.**

For example:

- * *Could the recipient organism survive in the environment in the event of a breach of laboratory containment?*
- * *Is the vector mobilisable?*
- * *Is the nature of the inserted gene such that its widespread dissemination in the environment would present particular environmental concerns e.g. a drug resistance gene or an intact provirus?*

7. Provisional Classification

Based on the hazards identified and the Biological Agent Hazard Group listed above, assign a provisional classification level (1, 2, 3, 4) (3A)

8. Comments:

9. RISK IDENTIFICATION

This is the estimation of the likelihood that the hazards will be realised. Assess the risk of Access, Expression and Damage, which together with an overall indication of which level of containment should be used.

9.1 Risk of Access

Assess the probability that a microorganism, or the DNA contained within it, will be able to enter the human body and survive there, or survive in the environment. The properties of the host organism and the vector need to be taken into account. Include in your assessment consideration of the following:

- * *Does growth require the addition of specific nutrients not available in humans or outside the culture media, and is sensitive to physical conditions/chemical agents, in man or environment, e.g. *E. coli* K-12, *Bacillus subtilis*, *Aspergillus oryzae*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*.*
- * *Is the microorganism a multiple auxotroph or other host, which is unlikely to persist in the gut, lung or survive outside the culture media, e.g. *E. coli* – DH5, JM109, TG2, XL-1Blue, *Pichia pastoris*. As the disablement of BL21 is unclear, unless it is rec⁻ it shouldn't be considered a multiple auxotroph.*
- * *Consider mobility of the vectors. Bom⁻ (Nic⁻), Mob⁻ and Tra⁻ vectors are non-mobilisable. They include *E. coli* vectors pUC, pGEM, pCAT, pBluescriptII, and *Bacillus* vector pUB110 and their derivatives. Bom⁺, Mob⁻ and Tra⁻ vectors are mobilisation defective. They include *E. coli* vectors pBR322, pGEX and their derivatives.*

Mobilisable vectors are Bom^+ , Mob^+ and Tra^+ . They include RP4, RSF1010, ColE1 and F.

- * Organisms known to colonise humans (e.g. wild-type *E. coli* or *Salmonella*) are given an access factor of 1. Organisms with little ability to colonise (e.g. the laboratory strain *E. coli* K-12) are given an access factor of 10^{-3} .

9.2 Risk of Expression

Assess the probability that the manipulated DNA, having gained access to the body, will be expressed as a polypeptide product. Maximum expression is given a probability of 1 and no expression a probability of 10^{-6} . For each gene, is there:

- * A deliberate in frame insertion of expressible DNA downstream of a strong promoter with the intention of maximising expression.
- * Insertion of expressible DNA downstream of a strong promoter with no attempt to maximise expression.
- * Insertion of expressible DNA into a site of limited promoter activity.
- * Insertion of expressible DNA at a site specifically engineered to prevent expression
- * Non-expressible DNA

What is the likelihood of harm being caused to a person or the environment by exposure to the GMM? Consider the scale of the work and the provincial containment level suggested above.

9.3 Risk of damage

Assess the probability that an expressed gene product can damage the host. A highly toxic protein (e.g. ricin) would have a damage factor of 1. A biologically active molecule (e.g. insulin) would have a factor of 10^{-6} , while a molecule with no foreseen biological effect would be assessed as 10^{-12} .

Overall risk factor

This is obtained by multiplying the three factors together (A x E x D).
The overall risk factor indicates the required level of containment.

Score	ACGM Containment level
$<10^{-15}$	1
10^{-12}	2
10^{-9}	3
10^{-6}	3 or 4
$>10^{-6}$	4

The overall risk factor:

ACGM Containment level:

10. What is the scale of the proposed experiments (e.g. volume of cell cultures)?

11. Define the containment level that will need to be used to control the risk (3A):

12. Waste Inactivation and Disposal, Disinfection and Spillage.

(i) How will you dispose of waste materials (both solid and liquid laboratory waste)?

For example:

- * Liquid-based waste material is autoclaved or treated with chemical agents.
- * Solid biological material is securely packaged and disposed of by incineration via a registered contractor.

(ii) How has each method for inactivation of GM waste been validated, what is the 'Degree of Kill' and what monitoring is carried out to ensure this?

Example:

- Autoclaving: Effectively 100% kill at this program as shown by microbiological testing
- Incineration: effectively 100% kill

(iii) What disinfection and spillage procedures are used?

Example:

- Routine Disinfection: Bleach / 70% Ethanol - work surfaces are cleaned daily
- Spillage: Bleach / 70% Ethanol

(iv) Does your laboratory avoid use of sharps? If the answer is no, how are these disposed of?

13. Check list covering other work procedures and relevant issues

Addition control measures may take the form of one or more specific measures taken from the list of measures that are recommended for the containment level that is one level higher than the one assigned. Thus, some projects may be assigned to containment level 1 with one or two additional measures taken from the requirements of containment level 2 e.g. the requirement that all work with infectious materials should be undertaken in a safety cabinet.

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

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- (ii) 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, which might make them more susceptible to infection (e.g. some kind of immunological defect)?
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- (iii) Will workers receive any vaccinations? Give details.
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- (iv) Which other precautions are necessary to minimise risks?
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14. FINAL CLASSIFICATION

Assign the final class of activity to all aspects of the procedure. This classification is directly related to the containment level required to control the risk. It may be necessary to assign the containment level above or below that suggested by the hazard assessment.

Indicate whether the facility is equipped to conduct activities at the containment level required.

Example: After assessing the risk involved in using the GMMs, the laboratory can be classified as a **Class 1** facility.

Responsible person/people:

Full names	Signature	Date

Section 2: Declaration by responsible person

- 1.** I am forwarding this proposal to carry out work in genetic modification with the authority and approval of the person (individual or corporate body) undertaking the activities notified in this form.

Name:

Position:

Signed:

Date:

- 2. Authority to make this application has been granted by**

Name:

In my capacity as (position in organisation)

Signed:

Date:

- 3. The information provided in this form is to the best of my knowledge accurate.**

Name:

Signed:

Date:

PART II:**THE INFORMATION GIVEN IN THIS PART MAY BE PLACED ON A PUBLIC REGISTER**

1. Details of facility where the work is to be carried out

Name of Organisation:

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Faculty (if applicable):

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Address:

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2. The purpose of the genetic modification (*brief description of proposed activities*) and the containment levels involved:

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3. List of the genetically modified organism(s) involved or intended to be involved:

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