Guidelines and Handbook

for

Institutional Biosafety Committees (IBSCs)

Prepared by

DEPARTMENT OF BIOTECHNOLOGY
Government of India

In association with

Biotech Consortium India Ltd., New Delhi

2nd Revised Edition May, 2011

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Foreword

The Department of Biotechnology (DBT) has been taking steps from time to time for providing guidance documents for various stakeholder particularly research scientists in complying with rules and regulations for recombinant DNA technology based products and processes, in line with mandate under "Rules for the manufacture, use/import/export and storage of hazardous microorganisms/ genetically engineered organisms or cells, 1989" notified by the Ministry of Environment and Forests (MoEF), Government of India under the Environment (Protection) Act, 1986.

In 2004, DBT had released "Handbook for IBSC Members" which has been widely circulated across the country. Over the past six years, DBT was in continuous touch with the IBSCs through workshops and online interaction. Keeping pace with the developments in biotechnology research, several new IBSCs have been also constituted. To strengthen the regulatory compliance it was felt that further statutory guidance is needed to harmonize the regulatory system at par with international standards. This second revised edition of the handbook has been restructured to provide information for compliance by IBSCs and processes to be followed. The restructured and updated handbook includes updated guidelines for IBSCs, a checklist for evaluating proposal and new formats for submission of applications to IBSC and Review Committee on Genetic Manipulation (RCGM). The views of various stakeholders have been taken before finalizing the guidelines and the same have been adopted by RCGM.

I am glad that Dr. K.K. Tripathi, Adviser, DBT and Member Secretary, RCGM has put in considerable efforts in the strengthening regulatory compliance by IBSCs. Assistance provided by BCIL particularly Dr. Vibha Ahuja, General Manager; BCIL has been extremely useful in managing DBT biosafety websites involving interactions with IBSCs and revising the Handbook and Guidelines for IBSCs.

I believe this second revised version of handbook which has a section of guidelines for IBSCs would be not only useful for the members of IBSCs but also familiarize the industry, scientists, policy makers and students with the updated regulatory procedures.

(M.K. Bhan)

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Prologue

As per the Indian regulations, organizations handling genetically modified organisms (GMOs) and recombinant DNA (rDNA) materials for research or production should constitute an Institutional Biosafety Committees (IBSCs) with the Department of Biotechnology (DBT) approval. In the regulatory framework, IBSC is one of the statutory body which operates directly from the premises of the institution and is responsible for proper implementation of biosafety rules, regulations and guidelines.

As an exercise to strengthen the functioning of IBSCs, DBT in association with Biotech Consortium India Limited (BCIL) prepared and circulated a "Handbook for IBSC Members" in 2004 which covered mainly the composition, functions and role of IBSCs. However, over the time it was found that there is need to update and revise the handbook as there is need of clarity in some sections such as checklist and application formats. In this second revised edition of the handbook, format for registration and renewal of an IBSC is introduced. The regulatory websites set up by DBT viz. http://dbtbiosafety.nic.in and http://www.igmoris.nic.in, have been also added where IBSCs can submit the information. The text of the "Guidelines for IBSCs" adopted by RCGM for ensuring administrative compliance by IBSCs as been provided. Checklist for review of applications has been made simpler for easy assessment by IBSCs. Appropriate formats for submission of applications at various stages of the development process of a GMO for healthcare/ industrial applications and agriculture/ environment applications have been added.

I am pleased to put my appreciation for the sincere efforts put in by Dr. Vibha Ahuja, General Manager, BCIL throughout the preparation of this document. I also acknowledge the useful inputs provided by the members of the RCGM and various stakeholders during the review process.

Overall this revised handbook is prepared with a view to be "user friendly" for the members of the IBSCs, scientists, policy makers, industrialists and students.

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Introduction

In India, GMOs and products thereof are regulated as per the "Rules for the manufacture, use/import/export and storage of hazardous microorganisms/ genetically engineered organisms or cells, 1989" (commonly referred as Rules, 1989) notified by the Ministry of Environment and Forests (MoEF), Government of India under the Environment (Protection) Act (1986). These rules are implemented by MoEF, the Department of Biotechnology (DBT), Ministry of Science and Technology and the State Governments through the six competent authorities notified under the Rules which are as follows:

i. Recombinant DNA Advisory Committee (RDAC)
ii. Institutional Biosafety Committee (IBSC)
iii. Review Committee on Genetic Manipulation (RCGM)
iv. Genetic Engineering Appraisal Committee (GEAC)
v. State Biotechnology Coordination Committee (SBCC)
vi. District Level Committee (DLC).

While the RDAC has advisory in function, IBSC, RCGM, and GEAC are involved in regulatory functions. SBCC and DLC are responsible for monitoring the activities related to GMOs in state/district level. RDAC, RCGM and GEAC are constituted at the central level by DBT and MoEF. IBSCs at all organisations working in the area of GMOs, SBCC in all states and DLCs in districts, wherever necessary.

Out of the above, the IBSC is the nodal point for interaction within an organisation for implementation of the biosafety regulatory framework. An IBSC is to be constituted by every organisation engaged in research, handling and production activities related to GMOs and each IBSC has a nominee appointed by DBT. The role of IBSCs is extremely important as it is a Statutory Committee that operates from premises of respective organisation. Functions of IBSCs have been elaborated in the "Recombinant DNA Safety Guidelines, 1990" and "Revised guidelines for research in transgenic plants, 1998" issued by the DBT.

Introduction

DBT has taken several initiatives to strengthen the functioning of the IBSCs (Box 1). Pursuant to issuing various guidelines in 1990 and 1998, DBT in association with Biotech Consortium India Limited (BCIL) organised a series of national consultations at six locations for the IBSC members and the DBT nominees with an objective to apprise them about their roles in greater depth and detail. A detailed background document was prepared and circulated in the meetings. The interaction between the faculty and IBSC members helped in clarifying the roles and responsibilities of IBSC members in general and the DBT nominees in particular.

The first edition of the "Handbook for IBSC Members" was prepared in 2004 for the IBSC members and DBT nominees of IBSCs covering the composition, functions, role in approval and a checklist for evaluating projects, on a case-to-case basis. A CD containing important biosafety regulations and guidelines for GMOs was also included in the Handbook for ready reference by the IBSC members. The handbook was widely circulated and well received by all stakeholders associated with research & handling of GMOs including scientists, industries, institutions, universities, students etc.

In the past six years, several new IBSCs have been constituted and a need has been felt to provide further guidance for strengthening the regulatory compliance by

Box 1: Initiatives by DBT for regulatory compliance by IBSCs

i. Guidelines: DBT has formulated various biosafety guidelines for research involving GMOs that include Recombinant DNA safety guidelines, 1990, revised in 1994, Guidelines for carrying out research in transgenic plants, 1998 and Guidelines for preclinical and clinical evaluation of rDNA vaccines, diagnostics and other biologicals.

ii. Workshops for IBSC members and DBT nominees in 2004: DBT in association with Biotech Consortium India Limited (BCIL) organised a series of six "National Consultations on Biosafety aspects related to GMOs for members and nominees of DBT on IBSCs" in 2004 at Bangalore, Chennai, Hyderabad, New Delhi, Mumbai and Jalna with an objective to interact with IBSCs representatives in evaluation and monitoring of the recombinant DNA projects. About 450 participants attended the consultations. Regulatory compliance at institutional level was identified as one of the important gaps and it was suggested that there was a need for extensive capacity building efforts.

iii. Handbook for IBSC members: DBT and BCIL prepared a handbook for IBSC members and circulated the same all over the country. The handbook explains in detail the roles

and responsibilities of IBSC members, procedures for setting up of an IBSC and evaluating the project proposals including a checklist for the same.

iv. CD on biosafety guidelines, rules, regulations and protocols: A CD has been prepared by DBT in association with BCIL compiling all guidelines, rules, regulations and protocols with various Government Notifications for the benefit of all the stakeholders.

v. Series of workshops for SBCCs, DLCs and IBSCs: MoEF and BCIL organised a "Series of six training workshops on biosafety issues for the members of State Biotechnology Coordination Committees (SBCCs), District Level Committees (DLCs) and Institutional Biosafety Committees (IBSCs)" across the country from April – June 2007 by BCIL in association with State Department of Environment, Agriculture, Health and Science & Technology at Chandigarh, Bhopal, Hyderabad, Pune, Bangalore and Chennai with an objective to apprise up-to-date information to the members of SBCCs, DLCs and IBSCs about provisions of the Cartagena Protocol on Biosafety and share views/experience of these regulatory committees.

Vi Web based database and online interactions with IBSCs: DBT operationalised two websites viz. http://dbtbiosafety.nic.in and http://www.igmoris.nic.in to facilitate interaction with IBSCs and information compilation and dissemination on rDNA activities in the country.

Vii Workshops for IBSCs in 2009: Interaction with IBSCs was again undertaken by DBT and BCIL through a "Series of six workshops for DBT nominees and IBSC members for strengthening regulatory compliance by IBSCs". These workshops were held at Mumbai, Kolkata, Bangalore, Hyderabad, New Delhi and Chennai. More than 400 IBSC members and DBT nominees participated in these workshops. The participants were also apprised of compliance requirements with respect to online information exchange websites established by DBT.

increasing number of IBSCs. Therefore, it has been felt necessary to update the handbook by preparing new set of guidelines, checklists and application formats for use by IBSCs. Accordingly, the second revised edition of the handbook has been prepared, which is the outcome of various initiatives by DBT for the benefits of IBSCs in particular and others in general. The handbook has been restructured and updated so as to be user friendly. Attempt has been made to include responses to several queries that are regularly posted to DBT as well to avoid inconsistencies in functions

of IBSCs by putting together a set of guidelines. A checklist has been provided for evaluating the applications by IBSCs. The new formats for submission of applications to IBSC and RCGM have been included alongwith guidance for submission of applications to RCGM. Accordingly, the second revised version has been renamed as "Guidelines and Handbook for IBSCs" and has three sections as indicated below:

- Guidelines for IBSCs
- Checklist for IBSCs
- Guidance and formats for submission of applications to RCGM

The handbook also has a CD containing softcopy of all relevant rules, regulations, guidelines and formats.

GUIDELINES FOR IBSCS

I

Guidelines for IBSCs

The following is the text of guidelines for IBSCs as adopted by Review Committee on Genetic Mainpulation (RCGM):

1. Purpose/Objectives

The purpose of these guidelines is to provide guidance to organisations that have Institutional Biosafety Committees (IBSCs) or intend to set up an IBSC in compliance with "Rules for the manufacture, use/import/export and storage of hazardous microorganisms/ genetically engineered organisms or cells, 1989" (hereinafter referred as Rules, 1989) notified by the Ministry of Environment and Forests (MoEF), Government of India under the Environment (Protection) Act, 1986.

As a statutory committee that operates from the premises of an organisation, IBSC is in a position to conduct onsite evaluation, assessment and monitoring of adherence to the biosafety guidelines with overall oversight of the regulatory process, at the institutional level. The decisions taken by the next higher committee i.e., Review Committee on Genetic Manipulation (RCGM), which operates from the Department of Biotechnology (DBT), Ministry of Science and Technology, Government of India are based on the applications submitted by the investigators with the approval of IBSC. Therefore,it is pertinent that IBSCs have expertise in evaluation, assessment and monitoring of projects and ensure compliance with the Rules, 1989, Recombinant DNA (rDNA) Safety Guidelines,1990 and other guidelines issued by DBT from time to time.

2. Scope

These guidelines describe the constitution, composition, role and functions of IBSCs. The guidelines provide information for compliance requirements by IBSCs and processes to be followed while dealing with genetically modified organisms (GMOs)/living modified organisms (LMOs) and rDNA materials in line with Rules, 1989 and guidelines issued by DBT from time to time.

3. Terminology

- **Biosafety Officer:** The Biosafety Officer is the designated officer appointed in case rDNA research involves biosafety level 3 or 4 containment facilities or large scale rDNA research.
- **Containment (adopted from rDNA safety guidelines, 1990):** The term "containment" is used to describe safe methods for managing infectious agents and/or regulated GMOs/LMOs/rDNA material in the laboratory environment where they are being handled or maintained
- **DBT:** Department of Biotechnology, Ministry of Science and Technology, Government of India
- **Genetic Engineering (as in Rules, 1989):** The technique by which heritable material, which does not usually occur or will not occur naturally in the organism or cell concerned, generated outside the organism or the cell is inserted into said cell or organism. It shall also mean the formation of new combinations of genetic material by incorporation of a cell into a host cell, where they occur naturally (self cloning) as well as modification of an organism or in a cell by deletion and removal of parts of the heritable material.
- **GEAC:** Genetic Engineering Appraisal Committee
- **Head:** The Head refers to the Head of an organisation involved in rDNA activities, e.g. Vice Chancellor of a university or other educational institute, Chief Executive Officer (CEO)/Managing Director usually of a body corporate, Director General/Director/Head of an Agency, Research Institution, Department, Division, Industrial Research and Development Unit or its equivalent
- **IBSC:** The Institutional Biosafety Committee (IBSC) is a statutory committee of an organisation undertaking rDNA activities, constituted as per provisions of Rules,1989 and chaired by the Head of the organisation or his designate (a suitable senior officer).
- **Incident:** This means unintended release, breach of containment, spill or occupational exposure to GMOs/LMOs/rDNA materials.
- **Principal Investigator:** The Principal Investigator (PI) is involved in conducting modern biotechnology research in an organisation. The PI is accountable to the IBSC and must comply with the appropriate research guidelines and all applicable laws and guidelines related to biosafety.

- **Recombinant DNA (as in rDNA safety guidelines, 1990):** Recombinant deoxyribonucleic acid (rDNA) by definition involves *in vitro* introduction of different segments of DNA (one being the vector and the others normally unrelated DNA sequences) that are capable of replication in a host cell either autonomously or as an integral part of host's genome and maintenance of their continued propagation. This will include all types of cell fusion, microinjection of DNA or RNA or parts of all of chromosomes, genetic engineering including self cloning and deletion as well as cell hybridization, transformation and other types of virus or pathogen introduction into unnatural host. The organisms involved may belong to these categories:

i. Intergeneric organisms
ii. Well defined organisms with non coding regulatory regions.
iii. Biological agents whose source of DNA is a pathogen.
iv. Organisms that are generally recognized as non-pathogenic and may imbibe the characteristics of a pathogen on genetic manipulation.

- **Regulatory Authority:** RCGM is the Regulatory Authority functioning in DBT to whom IBSCs shall report and Genetic Engineering Appraisal Committee (GEAC) is the apex Regulatory Authority functioning in MoEF responsible for authorizing environmental release.
- **RCGM:** Review Committee on Genetic Manipulation

4. Constitution of IBSC

i. Any organisation, which undertakes research, shall establish an IBSC to ensure that all activities conducted comply with Rules 1989 and various guidelines issued by DBT from time to time.
ii. The IBSC shall be registered with DBT.

5. Tenure of IBSC

i. Each IBSC shall be registered for a period of three years.
ii. The registration needs to be renewed after every three years.
iii. The request for renewal must be submitted 60 days in advance before the expiry of the tenure of IBSC.

6. Composition

6.1 IBSC membership

The IBSC shall have the following members:

- Head of the organisation or his designate (a suitable senior officer) as the Chairperson
- Three or more scientists engaged in rDNA work or molecular biology with atleast one outside expert in the relevant discipline.
- A member with medical qualifications - Biosafety Officer (in case of work with pathogenic agents/large scale use).
- A nominee of DBT.

One of the in house scientists may be designated as Member Secretary. The IBSC may comprise as many member as the organisation consider necessary to enable proper examining the type of activities with GMOs/LMOs and rDNA materials being undertaken with the organisation. There is no upper limit to the membership of IBSC.

6.2 IBSC Chairperson

The Head of the organisation or his designate (suitable senior officer) shall chair the IBSC. The Chairperson should represent the organisztion and preferably have knowledge and experience in scientific research pertaining to rDNA technology and GMOs/LMOs.

6.3 Appointment of IBSC Members

IBSC members are appointed by the Head of the organisation, and will serve a 3 year term unless they are appointed to complete the term of any member who cannot serve IBSC any longer because of reasons like resignation, retirement, transfer, suspension etc. Members may be reappointed at the end of each 3 year term. There is no limit to the number of terms a member may serve as an IBSC member. Membership can be annually reviewed by the IBSC Chairperson and Head of the organisation and appropriately modified based upon participation.

6.4 Biosafety Officer

The organisation must appoint a Biosafety Officer, if research is conducted on organisms that require special containment conditions (Biosafety Level 3 or 4)

or if large-scale rDNA research is conducted. This person is also a member of the IBSC and acts as a technical liaison between researchers and the IBSC. The Biosafety Officer should be adequately trained and be able to offer advice on specialized containment requirements.

6.5 DBT Nominee

Each IBSC has a nominee from DBT who oversees the activities to ensure that safety aspects are being fully adhered by the organisation. The DBT nominee serves as the link between DBT and the respective IBSC.

6.6 Changes in IBSC Membership

Any changes in IBSC membership/composition including the Chairperson will be notified by the IBSC Chairperson/Member Secretary to DBT within two weeks of the new appointment/discontinuation. Such notice should include a revised list of members, contact details and background information on each new member.

6.7 Use of Experts/Consultants

IBSC may use qualified experts/ consultants from within or outside organisation for advice and information, as and when required. Participation of such external experts/consultants in meeting should be recorded in the minutes.

7. Procedure of registration/renewal

7.1 Registration of IBSC

Every organisation setting up an IBSC needs to identify the members as listed in section 6.1. The request has to be submitted to DBT in prescribed proforma along with overview of the organisation and brief bio-data of the proposed members including qualifications, affiliation and relevant experience. DBT then identifies and nominates an appropriate representative as a DBT nominee and communicates the same to IBSC Chairperson. With this the IBSC of the organisation gets registered.

7.2 Renewal of IBSC

The procedure for renewal of an IBSC is similar to registration process. The format of renewal has been prescribed by DBT and the same should be used for

renewal of IBSC registration. The requirements with respect to list and background of proposed members etc. are the same as for registration.

8. Role of IBSC in approval

The role of IBSC in research, large-scale experiments/ production/field release and import and shipment shall be as under:

8.1 Research activities related to rDNA technology: IBSC has to review all recombinant research carried out by an organisation depending upon the category of experiments, IBSC can simply note the information provided by PI, give permission before start of the experiments or forward it to RCGM for approval as per the Recombinant DNA Safety Guidelines, 1990 of DBT.

- Category I experiments involving self cloning, using strains and also inter species cloning belonging to organism in the same exchanger group etc. are exempt for the purpose of intimation and approval.
- Category II experiments falling under containment levels II, III and IV, large scale use of recombinants made of self cloning in systems belonging to exempt category etc. require prior intimation to IBSC.
- Category III experiments involving toxin gene cloning, cloning of genes for vaccine production, use of infectious animals and plant viruses, self fusion experiments, field testing and release of GMOs etc. require review and approval of IBSC before commencement.

Different levels of containment have been prescribed for different categories of rDNA experiments in the Guidelines. IBSC should allow genetic engineering activity on classified organisms only at places where such work can be performed as per Guidelines and containment facilities.

Provision of suitable safe storage facility of donor, vectors, recipients and other materials involved in experimental work should be made and may be subject to inspection for accountability on biosafety.

8.2 Research activities related to transgenic plants: In case of research activities related to transgenic plants, IBSCs shall follow "Revised Guidelines for Research in Transgenic Plant, 1998" by DBT (http://dbtbiosafety.nic.in). Routine recombinant DNA experiments fall in Category I and need only

intimation to the IBSC in the prescribed proforma. Category II include lab and greenhouse/ nethouse experiments in contained environment where defined DNA fragments that are non pathogenic to human and animals are used for genetic transformation of plants. Permission for performing Category II experiments is provided by IBSC but the decision of the IBSC needs to be intimated to the RCGM before execution of the experiment and RCGM would put this information on record. Category III pertains to high risk experiments where the escape of transgenic traits into the open environment could cause significant alterations in the biosphere, the ecosystem, the plants and animals by dispersing new genetic traits, the effects of which cannot be judged precisely. All experiments conducted in greenhouse and confined field conditions not belonging to the above Category II types, would fall under Category III risks. Such experiments could be conducted only after clearance from RCGM and notified by DBT

8.3 Large scale trials and production: In cases for conduct of field trials and large scale production, IBSC has to verify the information being forwarded to RCGM and GEAC in terms of physical containment conditions, categorization in terms of risk assessment etc., as further reviews by these regulatory committees depends on the review of the IBSC on the submissions made.

IBSC has to recommend emergency plan in case of large-scale operations, as and when required, which would be then approved by competent authorities i.e. RCGM and GEAC. Emergency plan shall include methods and procedures for handling large volumes of cultures and organisms for production, transport, storage or disposal etc.

8.4 Import and transfer/shipment

- The interstate transfer/shipment of indigenous etiological agents, diagnostic specimens and biological products need clearance of IBSC and is subject to appropriate packaging, labeling and shipping requirements.
- The import permits of regulated materials for research and specifying conditions under which the agent or vector is shipped, handled and use are issued by RCGM while large scale imports regulated material for environmental and industrial use are regulated by GEAC.

- In case of plants, the import is routed through the Director, National Bureau of Plant Genetic Resources (NBPGR) on the basis of the import permit issued by the RCGM Secretariat, based on recommendations of the RCGM. However, all these proposals need to be submitted by the PIs through their IBSCs.

9. Functions

9.1 IBSC

The responsibilities of the IBSC include, but are not limited to the following:

- Review and clearance of project proposals falling under restricted category and as per guidelines issued by DBT from time to time and elaborated above in Section 8.
- Tailoring biosafety programme to the level of risk assessment.
- Assess and monitor the research facilities, procedures and experts involved in GMOs/LMOs and rDNA research.
- Inform the Principal Investigator about IBSC review, approval or rejection of their projects
- Information of all relevant activities involving the use of GMOs/LMOs and rDNA research to the RCGM.
- Ensure that the information provided in the application form is correct and complete.
- Provide guidance to Principal Investigator on the issues related to biosafety while using GMOs/LMOs and rDNA research including safety of all the members associated with the research activity.
- Assess field experiments to ensure that the proposed risk assessment, risk management and emergency plan are sufficient.
- Review the emergency plan proposed by the Principal Investigator for responding to an accidental release of a GMO and those adopted to meet any exigencies. Copies of site emergency plan to be submitted to RCGM, GEAC, State Biotechnology Coordination Committee (SBCC) or District Level Committee (DLC) as the case may be, as per Rules, 1989.
- Review and report to the Head of the organisation and to Member Secretary, RCGM of any non-compliance of guidelines / problems.

In addition, the Chairperson, Member Secretary, Biosafety Officer and DBT nominee of IBSC have specific functions. Further the Principal Investigator(s) of the project(s) have significant role to play in complying with he regulatory framework. The responsibilities of each of above are elaborated below:

9.2 Chairperson

- The Chairperson should preside over the IBSC meetings and serve as the contact with all regulatory agencies to help liaise between the organisation and the IBSC. The Chairperson of IBSC may designate a member of the IBSC to serve as Acting Chair in his/her long term absence.
- Have awareness of all requirements regarding compliance with the Rules, 1989 and any related regulations regarding GMOs/LMOs/rDNA materials and ensure that the biosafety guidelines are followed in his organisation.
- Ensure that the facilities at the organisation are sufficient to meet the containment levels stipulated for rDNA products and processes, as per the guidelines.
- Make sure that regular meetings of IBSC are held to review recombinant research projects in the organisation and open discussion takes place amongst the members in the meetings and the views of external members as well DBT nominee are recorded sincerely.
- Provide leadership and support that laboratory personnel receive appropriate training prior to the initiation of research projects (i.e. experimental procedures).

9.3 Member Secretary

- The Member Secretary shall be responsible for all reporting and communication with respect to functioning of IBSC in an organisation
- Maintain documents, agenda minutes of meetings and other related papers for proper record keeping
- Organising meetings and provide technical advice to Principal Investigator about safety procedure and containment facility.

9.4 Biosafety Officer

- Act as a focal point for compliance with rDNA safety guidelines, good lab practices, biological containment etc

- Ensure that measures are in place to prevent the accidental escape of regulated GMOs/LMOs and rDNA materials.
- Undertake periodic laboratory inspections.
- Assist Investigator in developing emergency plans for containment and clean up accidental spills; investigates and reviews recombinant DNA lab accident
- A report from the officer may form part of the IBSCs annual report.

9.5 Principal Investigator

All recombinant research projects carried out by an organisation involving the use of GMOs/LMOs or rDNA materials should have a Principal Investigator (PI). It is the duty of the PI to apprise the IBSC about the nature of the experiments being carried out. Depending upon the risk category, the PI has to inform the IBSC, seek permission of IBSC before starting the experiments or seek permission of the RCGM through its IBSC.

Based on the nature of the GMOs/LMOs and rDNA materials, the PI determines the proper containment level for the project and, in accordance with the guidelines, develops the necessary experimental protocols. This information is then submitted to IBSC for review. The responsibilities of PI are summarized below:

- to make an initial determination of the required levels of physical and biological containment in accordance with the stipulated guidelines.
- to submit the initial research protocol and any subsequent changes (such as changes in the source of DNA or host vector system) to the IBSC for review and approval.
- to ensure that no work is initiated until the research project has been approved by the IBSC and has met all requirements of DBT guidelines.
- to communicate with IBSC throughout the conduct of the project.
- to ensure safe conduct of the rDNA experiments in his laboratory.
- to make available the protocols that describe the potential biohazards and the precautions to be taken to all laboratory staff.
- to instruct laboratory staff about the practices and techniques required to

ensure safety, and the procedures for dealing with accidents including the reasons and provisions for any precautionary medical practices advised or requested (e.g. vaccinations or serum collection).

- to supervise the performance of the laboratory staff to ensure that the required safety practices and techniques are employed.
- to undertake corrective measures promptly for any work errors and conditions that may result in the release of recombinant DNA materials.

9.6 DBT nominee

The duty of the DBT nominee is to ensure that:

- The IBSC has been constituted as per the norms.
- The stipulated rDNA Safety Guidelines are strictly followed in the organisation/institution.
- The IBSC meets regularly, at least twice in a year to review the ongoing activities and provides annual reports to RCGM in the prescribed proforma.
- All the activities are within the purview of the guidelines and in the knowledge of RCGM.
- The DBT nominee is also expected to guide the IBSC on biosafety issues.

10. IBSC meetings

10.1 Regular meetings

The IBSC shall meet as required. However each IBSC has to meet at least twice in a year to review and approve the rDNA projects in an organisation. It is important that the Chairperson and Member Secretary ensure that regular meetings take place. More than two meetings may be held as per requirement of the projects. The IBSC members are expected to look into the following aspects during the meetings:

- Action taken on the decisions of earlier IBSC meetings.
- Assessment of work elements and approval as per risk category of organism involved.
- Evaluation of projects and direction for submission to appropriate agencies for statutory approvals.

- Inspection of containment facilities, unit process areas, greenhouses etc. and preparation of reports for regulatory agencies.
- Review the medical reports of employees
- Examining and recommending procedures and other approval requirements.

10.2 Emergency meetings

The Chairperson may call an emergency meeting of the IBSC to address any urgent issues such as non-compliance or unexpected events involving GMOs/ LMOs/ rDNA materials in an organisation.

10.3 Documents to be reviewed

Prior to the regular meeting, each member should be sent a copy of the documents to be reviewed at the meeting, in addition to other information to be discussed. The prescribed formats for information on projects to the IBSC and RCGM should be used appropriately.

10.4 Attendance and Quorum

Attendance of members at IBSC meetings is mandatory. Members who are unable to attend the meeting should inform the Chairperson, IBSC and provide a written summary of their review and any comments to the IBSC. It is mandatory to provide the duly signed attendance sheet as part of IBSC minutes, while submitting the minutes of IBSC meeting to the Member Secretary, RCGM.

At least 50% of the IBSC members along with DBT nominee must be present to conduct the meeting. The final approval or disapproval of non-exempt projects of GMOs/LMOs/rDNA materials requires a majority vote by IBSC members and DBT nominee. If a quorum is lost at any time during the meeting, the meeting should be adjourned and no further action should be taken by the IBSC until a quorum is re-established or a new meeting is appropriately convened.

10.5 Minutes of IBSC meetings

Minutes of IBSC meetings should include the following information:

i. Attendance of members and invitees, if any.

ii. IBSC's review and decisions on all applications considered in the meeting including modifications to project proposals,if any.

iii. Remarks on suitability of facilities with respect to containment requirements after inspection of GMOs/LMOs/rDNA facilities and suggestions, if any.

iv. Signatures of the Chairperson and DBT nominee is compulsory otherwise minutes will be treated as an invalid.

v. The minutes should clearly indicate about discussions and decisions taken during the meeting.

The intent of the minutes will be to provide sufficient detail about discussions on these matters and to document the IBSC's rationale for particular decisions taken.

11. Conflict of interest

IBSC members who have a conflict of interest in a project should not be present during the IBSC's initial or project extension review deliberations on the project. This might be their own proposal, or a proposal in which they are co-investigators, or in which they or a family member has a financial interest. Minutes should record the information on such members who have declared a conflict of interest.

12. Confidentiality

All members including DBT nominee and external experts are expected to maintain confidentially of the proposals and other related information made available to them for review, reference or discussion and not divulge any confidential or Intellectual Property (IP) or commercial business information (CBI) of an applicant/organisation/institute acquired as a result of review of such proposals and subsequent discussions. IBSC members are also expected to respect the confidential nature of the opinions expressed by other IBSC members or invited experts during discussions in the meetings or provided in written form and not divulge to any person, press or media.

If desired, IBSCs can sign a confidentiality agreement with the members including DBT nominee and/or external experts so as to ensure confidentiality of applications, issues and other matters placed before an IBSC.

13. Reporting requirements

13.1 Submission of Annual reports: Each IBSC has to furnish an annual report (in the month of January not later than 31st January) to RCGM in prescribed proforma regarding the observance of the safety guidelines including the progress on the ongoing projects in the organisation.

13.2 Information for biosafety websites: Each IBSC is required to provide information for the two regulatory websites set up by DBT as indicated below:

i. Biosafety Regulatory Website (http://dbtbiosafety.nic.in)

- Each IBSC is provided by DBT with a web account on the website http://dbtbiosafety.nic.in. The web account contains information about contact address, composition and agenda and minutes of meetings of IBSC etc. IBSCs are required to keep their web account updated and therefore any changes in contact details, head of the institution, concerned officer, members or DBT nominee should be promptly updated. Agenda as well as minutes of each IBSC meeting should be entered preferably within a week of holding the meeting.
- To facilitate the updation, each IBSC is provided with an account name by the web administrator. The account may be managed by the Member Secretary IBSC or any other person designated with the responsibility. Further information about how to update the web account is provided on the website itself.

ii. Indian GMO Research Information System (IGMORIS) Website (http://www.igmoris.nic.in)

- IBSCs are required to send information on projects/activities being undertaken by them regularly as and when new projects/activities are initiated (at least twice in a year in conjunction with IBSC meetings) for updating the information on the website. The required questionnaire for the above information is available on the Indian GMO Research Information System (IGMORIS) website (http://www.igmoris.nic.in). Further any changes with respect to head of the organisation, contact persons or contact details should be immediately communicated to DBT for necessary changes on the website.
- IBSCs are also required to submit one page brief write up containing brief

information about their organisation and various activities with a focus on projects involving rDNA technology. IBSC may review the information about their activities and provide regular updates reflecting new projects, new areas of research and other achievements

13.3 **Reporting for incidents and spills:** It is necessary that any incidents within an organisation such as non-compliance of the biosafety guidelines or any significant research-related accidents and illnesses (e.g. exposure to any uncontained GMOs/LMOs/rDNA materials, or contamination from equipment failure or a potential or overt exposure in the BSL-3 or BSL-4) be reported by the PI to the IBSC Chairperson using the Incident Reporting Form within 24 hours. PI is responsible for reporting any incident by submitting the Incident Reporting Form to RCGM within 48 hours from the incident. This form should be signed by Chairman, IBSC before submission.

These form(s) should be sent to the following address:

Member Secretary, RCGM
Department of Biotechnology,
Ministry of Science & Technology, Government of India
Block-II, CGO Complex, Lodi Road, New Delhi – 110 003

If deemed necessary, RCGM may also recommend that IBSC inform the incident to GEAC, SBCC and DLC or external agencies such as the local public health departments, state agencies, and the relevant funding bodies.

14. IBSC records

Each IBSC has to maintain the following records (in hard and soft copies) for future references.

i. Approved and duly signed minutes of IBSC meetings including attendance sheets.
ii. Annual report of all ongoing rDNA projects.
iii. Information about the projects approved by IBSC and related enclosures/ attachments.

iv. Applications forwarded to RCGM or GEAC

v. Other documents such as statements regarding conflict of interest, confidentiality agreements with DBT nominee and/ external experts etc.

15. Persons responsible for compliance

The responsibility for biosafety at an organisation rests with the Head of the organisation and PI, who obtains, possesses or uses GMOs/LMOs/rDNA materials. IBSC provides guidance to ensure compliance. Any possession and/ or use of these materials at the organisation must be conducted with appropriate safeguards against environmental release.

15.1 Head of the Organisation

The head of the organisation is responsible for compliance with Rules, 1989 and other related regulations regarding rDNA research. The head maintains ultimate responsibility for the safe conduct of activities involving GMOs/LMOs/rDNA research.

15.2 Principal Investigator (PI)

The PI is required to comply with the appropriate research guidelines and all applicable laws related to biosafety and is accountable to the Head and IBSC .

Laboratory Personnel (Technician, Technologist, Student, Post-doctorate) Laboratory personnel must:

i. Follow all safety guidelines and establish good laboratory practices. They must work within the assigned biological safety containment level and use personal protective equipment as recommended by the PI.

ii. Immediately notify the PI or BSO of any health condition that may be due to their work in the laboratory or any health condition that may be compromised prior to the initiation of a research project (i.e. pregnancy, immunosuppression).

iii. Follow all practices and procedures as provided by the PI and BSO, and ensure strict compliance with all required biosafety regulations and guidelines.

iv. Report problems, procedural mistakes, spills, etc. to the PI, and if necessary to the BSO, as soon as they occur.

v. Report to the PI, BSO or IBSC on non-compliance of biosafety guidelines or policies.

16. Addressing noncompliance

16.1 Noncompliance by Principal Investigator (PI)/ Organisation

The IBSC can address non-compliance to the Rules, 1989 or to the organisation's policies and procedures and any other relevant legal requirements. Non-compliance can result in the IBSC taking one or more of the following actions:

i. Suspension of the use of GMOs/LMOs/rDNA materials.

ii. Cessation of the approval for use of the GMOs/LMOs/rDNA materials.

iii. Confiscation and/or destruction of the GMOs/LMOs/rDNA materials.

iv. Any other action necessary to protect the public and/or the organisation, including suspending the relevant research activity.

v. Reporting to the RCGM.

16.2 Noncompliance by IBSCs

The registration of an IBSC can be cancelled by DBT in case IBSC does not comply with stipulated guidelines, including reporting requirements. If annual report of an IBSC is not received for two consecutive years, the registration will automatically laps and the organisation shall have to re-intiate the process of registration of its IBSC.

17. Training

17.1 Training of IBSC Members: All members of the IBSC should receive initial mandatory and refresher training on biosafety, the Rules, 1989, rDNA guidelines and related regulations and familiarise themselves with IBSC guidelines and institutional policies. In addition, IBSC members should receive refresher training on any changes to national guidelines. All such training will be organised by IBSC with commitment from the organisation

and guidance from RCGM. It is the responsibility of the IBSC Chairperson to arrange for providing this training.

17.2 Training of Laboratory Personnel: General biosafety training is mandatory for all individuals conducting research with GMOs/LMOs/rDNA materials. Such training may be organised by the organisation itself. Individual researchers must report to the IBSC that they have undergone training or have adequate experience in biosafety and Good Laboratory Practices. This includes knowledge in handling and management of incidents/accidents in the facility and information on when and how to report laboratory incidents. Individuals proposing to work in BSL-3 or BSL-4 containment must have specific BSL-3 laboratory training.

18. Laboratory inspections

The IBSC will inspect laboratories using checklists. Problems are to be reported to the PI for remedial procedures and, if necessary, to the higher relevant authority in the organisation. Inspection reports should be maintained on file in the IBSC.

For routine inspections, relevant authorised personnel, such as IBSC members, as well as representatives and officers authorised by the regulatory authorities should be allowed access to laboratories that are involved in activities with GMOs/ LMOs/ rDNA materials.

19 Security of GMOs/LMOs/rDNA materials

Authorised access and proper storage of biological materials is very important and should be taken seriously. The PI and all associated personnel must be conscientious in controlling these materials and should be held accountable for them. Access to biological materials should be limited to authorised personnel only. The PI, depending on the risk group of GMOs/ LMOs and rDNA materials, should develop a plan to protect the security of the material in question . The plan might include measures such as additional locks for laboratories, chain-of-custody forms within laboratories to track materials, inventories of biological materials, logs of access etc. The SOPs for use of biological materials should be in place including access to GMOs/LMOs and rDNA materials

for routine cleaning, maintenance, and repairs, restricting unauthorised persons, addressing loss of keys, passwords and any other secured information and material etc..

20. Disposal

IBSC may review the disposal methods as potentially hazardous biological materials and GMOs/LMOs/rDNA materials are to be considered as "regulated waste" and should be disposed of in a manner consistent with rDNA safety guidelines and other stipulated guidelines issued from time to time.

CHECK LIST FOR IBSCS

II

Check List for IBSCs

As indicated in the above mentioned guidelines, IBSC is responsible for evaluating activities involving the use of GMOs/LMOs and rDNA material in an organisation.

The aspects to be reviewed by IBSC broadly include scientific considerations and availability of appropriate facilities. In addition, DBT nominee is also expected to review the organisational set up, facilities, and status of other approvals required/obtained etc. of rDNA research projects on a case-to-case basis.

A checklist is presented here to assist IBSC members in reviewing the research proposals from investigators. It may be noted that this list is indicative. Specific additions/deletions or modifications would need to be made to suit the requirements of each project on a case-to-case basis.

1. Scientific Considerations

Safety assessment is a scientific process that makes use of the best up-to-date scientific knowledge and experience. Although details of safety assessment may vary from case-to-case, there are some logical steps that need to be followed. Information requirements for review of project proposal by an IBSC are given in Table-1 and elaborated in the context of safety assessment in the text below. It may be noted that information requirements and analysis shall depend on the stage and application area of a proposal.

Check List for IBSCs

Table 1: Information required for safety assessment of a GMO

Particulars	Information Required
Molecular Biology Details	
Characteristics of donor organisms	• Origin/source and taxonomic classification • Nature of pathogenicity and virulence, infectivity or toxicity, its host range and stability of these traits
Characteristics of host/recipient organisms	• Origin/source and taxonomic classification • Information on reproductive biology, including, growth and development, floral biology, reproductive cycle (asexual/sexual) details, dissemination of seeds • Nature of pathogenicity and virulence, infectivity or toxicity, its host range and stability of these traits • Degree of relatedness including evidence of exchange of genetic material between donor and recipient organisms or any other organisms
Characteristics of gene construct	• Description of all genetic materials used for modification of GMO, including, their sources, sizes, coding and non coding regions, orientation, etc. • Physical map (including coding regions, promoters and enhancers, marker genes, antisense genes) • Nucleotide sequence of intended insert and its function/s
Characteristics of vector and method of transformation	• Nature, source and function of vector • Method of transformation and detailed description of transfer method • Selection method for transformant • Type of insertion (complete or partial) and number of integration sites • Confirming integrity and fidelity of the insert • Determining production of fusion protein and its location in recipient organism
Characteristics of transformed/ modified organism	• Genotypic characters including characterization of site of modification of recipient genome,

Particulars	Information Required
	regulation and stability of inserted DNA, frequency of mobilization of inserted DNA and/ or genetic transfer capability
	• Phenotypic characters including taxonomic characterization, colonization potential, antibiotic resistance, infectivity, production of toxins, allergens, antinutrients or any other metabolites and its host range
	• Expression and properties of the gene product including copies /number of new gene(s), rate and level of expression, activity of expressed protein, allergenic/toxic hazards of the product
	• Confirmation of inheritance of new trait(s) over multiple generations
Human Health Considerations	
Toxicity	• Comparison of the amino acid sequence homology of the newly expressed protein with the known protein toxins and antinutrients
	• Animal toxicity studies
Allergenicity	• Comparison of the amino acid sequence homology of the newly expressed protein to known protein allergans
	• Heat stability and susceptibility of the expressed protein to pepsin digestion
	• Studies such as skin sensitization in animals
Nutritional analysis	• Changes in the level of key nutrients, natural toxicants or anti nutrients, secondary metabolites, physiologically active (bioactive) substances, etc.
Environmental Considerations	• Changes in the growth, habit, life cycle, biomass and reproductive characteristics, response to biotic and stresses , changes in aggressiveness potential and weedy characters, non target adverse effects etc.
	• Disposal of biological material

1.1 Molecular biology details

Recombinant DNA technology basically uses three components for genetic manipulation i.e. the selected gene from the donor organisms, the vector used for transfer of the gene and the host organisms. Therefore, the first step in risk assessment is to examine these three entities, followed by the resultant gene products and the genetically modified organism (GMO).

i. *Characteristics of the donor organisms*

If the donor organism is merely used as a source of well-characterized DNA for a selectable phenotype or a promoter or other control sequence, the characteristics of the donor are not very important for the risk assessment. If, however, the insert contain genes which are biologically active, producing toxins or virulence factors, then information from the donor organism is extremely important and of risk consequence and its assessment. The construction of cDNA or genomic libraries helps in consideration of all the possible hazards associated with the donor organism.

Although, the characteristics of the donor organism are of less relevance for the risk assessment than those of the host, the hazard group of the resultant would be generally higher of the two within which the host and donor fall.

ii. *Characteristics of the host/recipient organisms*

A thorough knowledge of the host or recipient organism is extremely important in assessment of the risks of the GMOs particularly keeping in view the concept of substantial equivalence as a starting point. The identity of the host must be established and the taxonomy well understood. There should be adequate and documented experience of the safe use of the host organism. The characterization of the host provides the starting point for the risk assessment. The assumption that is generally taken is that, the level of risk associated with the modified organism is at least as great as that of the host organism (until proved otherwise).

In case of microorganisms, the pathogenicity of the organism is extremely important for the risk assessment and subsequent categorization. The host must be evaluated to determine that it is not pathogenic. Infection by a microorganism followed by disease depends on its ability to multiply in the host and on the host's ability to resist or control the infection. The microorganisms have been

categorized with four groups based on the infectivity potential (pathogenicity) for humans out of which the first group is that of non-pathogens (Table 3). This categorization is generally applicable only for the assessment of containment requirements as greater containment is required to control the organism in the higher hazard groups to ensure that the organism does not infect those working with it.

Table 3: Categorization of microorganisms based on pathogenicity

Hazard Group 1	Organisms that are most unlikely to cause human disease
Hazard Group 2	Organisms capable of causing human disease and which may be a hazard to laboratory workers, but are unlikely to spread to the other co-workers of sister laboratories or community. Laboratory exposure rarely produces obvious infection or severe disease symptoms and effective prophylaxis or effective treatment is usually available
Hazard Group 3	Organisms that cause severe human disease and present a serious hazard to laboratory workers. They may present a risk of spread to the community, but there is usually effective prophylaxis or treatment available
Hazard Group 4	Organisms that cause severe human disease and are a serious hazard to laboratory workers. They may present a high risk of spread to the community, and there is usually no effective prophylaxis or treatment except quarantine measures.

The details of microorganisms falling into each category are given in the Recombinant DNA Safety Guidelines, 1990.

Some organisms have been frequently used in rDNA technology experiments and their characteristics have been described in detail e.g. *E. coli* or *Saccharomyces cerevisae*, about which a great deal is known. Further, no pathogenic strains of bakers' or brewers' yeast have ever been observed. This type of familiarity allows some confidence in attempting to identify risks associated with their modification. Some strains, for example, *E. coli* K12 has been disabled to remove some of the factors that might be associated with pathogenicity (wild type *E. coli* is a Hazard Group 2 pathogen). The factors which have been lost include the cell-surface K

antigen, part of the LPS side chain, the adherence factor (fimbriae) that enable adherence to epithelial cells of human gut, resistance to lysis by complement and some resistance to phagocytosis. This variant of *E.coli* is a common host organism for genetic modifications within the laboratory.

In case of plants being used as the hosts for genetic manipulation, additional factors such as potential invasiveness of the species need to be considered. Plant species have different geographical ranges and estimates of invasiveness may vary in different regions. Plants and plantation crops can be divided broadly into six categories in accordance with their invasive potential:

i. Crops that have no compatible relatives, carry few weediness traits (less than 40 percent), and do not persist in natural environments.

ii. Crops that have no compatible relatives, carry intermediate numbers of weediness traits, rarely escape, and do not persist in natural environments.

iii. Crops that have no compatible wild relatives, carry many weediness traits, and can escape and persist in natural environments.

iv. Crops that have compatible relatives, carry few weediness traits, and can escape but do not persist in natural environments; their compatible relatives also carry few weediness traits and dot not aggressively spread

v. Crops that have compatible relatives, carry intermediate numbers of weediness traits, and can escape but do not persist in natural environments; their compatible relatives also carry few weediness traits and do not aggressively spread.

vi. Crops that have compatible wild relatives, carry many weediness traits, and can escape and persist in natural environments; their compatible relatives also carry many weediness traits and aggressively spread.

The relative risk of using a transgenic crop will increase with the degree of invasiveness.

The relatedness between the host and the donor organisms is also important in the risk assessment particularly with respect to exchange of genetic material between them as well as with other organisms.

iii. ***Characteristics of the insert/ gene construct***

The properties of the insert are extremely important in risk assessment of GMOs. For example if the information encodes a toxic gene product, or one which is known to be likely to modify the pathogenicity of the organism into which it is inserted, there is greater risk from the GMO. However, if the gene product is non-toxic and is not the one which may pose a risk to the people working with the organism in containment, the risk management will largely be based on the pathogenicity of the host organism. In case of plants, the transgenes for herbicides and pest resistance need more careful scrutiny as compared to the ones that are selectively neutral in the natural environment.

Individual components used in the preparation of the construct i.e. promoters, enhancers, marker and terminator genes also need to be carefully reviewed.

iv. ***Characteristics of the vector and method of transformation***

The vector has to be characterized both for its own potential for pathogenicity and for its ability to transfer the insert to organisms other than the intended horizontal transfer. The function of the genetic material on the vector should be known as this would ensure that the vector is free from sequences that could be harmful to humans or the environment. The vector should be limited in size as much as possible to the genetic sequence required to perform the intended functions. This decreases the probability of introduction and expression of cryptic functions or the acquisition of unwanted traits. The presence of genes coding for antibiotic resistance might be of concern, although, for most of the vectors the antibiotic resistance is already common in the environment.

The methods of transformation used for introducing the required gene should be considered for the risk assessment of the modified organism. For example, in case of plants, the two principle methods of transformation that are widely used are the Agrobacterium mediated transformation and particle bombardment. Whereas Agrobacterium mediated transformations result in a low transgene copy number, minimal rearrangement and higher transformation efficiency, particle bombardment causes extensive rearrangements to transformed sequences.

v. ***Characteristics of the modified organism***

Molecular characterization of the GMO is used to provide information about the composition and integrity of inserted DNA, the number of copies of inserted DNA, the number of sites of insertion and the expression level of novel proteins over time and in different tissues in case of plants and animals. Molecular characterization can provide useful information but cannot by itself answer all questions on risk assessment and safety of GMOs.

The inheritance and stability of each introduced trait i.e. functional in the modified organism must be determined. For each novel trait the pattern and stability of inheritance must be demonstrated as well as the level of expression of the trait by estimation and analysis of the protein. If the new trait is one that does not result in the expression of new or modified protein then its inheritance will have to be determined by examining the DNA insert directly or by measuring RNA transcript production.

The first presumption for safety assessment of GMO is that the modified organism is as hazardous as compared to the host. For example, work with modified haemolytic *Streptococci* will proceed in the laboratory in a similar way as with other *Streptococci* of this type and of known pathogenicity. However, more precautions are normally required for modified organisms as introduced external DNA might increase the hazard usually attached to these haemolytic *Streptococci*. Formally, such increased potential of the hazard is expressed by classification of the manipulated strain in higher risk category. The formulation "might increase" is important since it reflects the lack of familiarity with the new strain. In some cases it may be observed that the opposite happens i.e. the new strain will be less invasive, the haemolysis less expressed. In short - the strain will represent less hazardous to human health. Nevertheless, the new strain has to be treated as more dangerous until confirmed otherwise.

Risks associated with a GMO can be assessed by considering three factors i.e. access, damage and expression. Access is a measure of the probability that a modified organism, or the DNA contained within it, will be able to enter the human body and survive there or escape into the environment as the case may be. It is a function of both host and vector. The properties of the vector, particularly mobilization functions need to be taken into account. Expression and damage are usually associated with the insert and the gene product.

Expression is a measure of the anticipated or known level of expression of the inserted DNA. If the 'gene' inserted is intended to be expressed at a high level, for example, by deliberate in-frame insertion down-stream of a strong promoter, expression is likely to be high. If the insert is simply there to allow probes to detect the DNA, and is non-expressible DNA, i.e. with no foreseeable biological effect or gene containing introns, which the host is incapable of processing, then the expression factor will be low. Examination of the modified organism determines the actual expression, which may be higher or lower than expected.

Damage is a measure of the likelihood of harm being caused to a person by exposure to the GMO, and is independent of either expression or access. It is associated with the known or suspected biological activity of the DNA or of the gene product. The activity of the organism, which results in any toxic, allergenic or pathogenic effect need be taken into account within this parameter. It may be noted that the biological activity of a protein is dependent on the host cell system in which it is expressed. An oncogene expressed in a bacterium will have no discernible effect, but when it is present in a human cell, problems may arise. The full biological function of many gene products requires post-translational modification, which will not occur within a bacterial cell normally. The potential biological activity of the gene product should be considered in the context, where and how it has been expressed and the effect on its structure and activity and the mode of manufacture.

Once an estimate of each of these parameters has been made, they may be combined. The result provides a qualitative measure of the risk, and allows a containment level to be assigned for the use of the organism.

The categorization scheme based on safety assessment has been given in Recombinant DNA Safety Guidelines, 1990 which should be referred to for evaluating the containment requirements as well as approvals to be taken.

1.2 Human health considerations

Impact on human health is studied by analyzing the modified organism for the risks of toxigenicity, allergenicity, pathogenicity, teratogenicity etc. as relevant in a particular situation. Assessment procedures and criteria vary in each case of genetic modification carried out in microorganisms, plants, animals etc. and products thereof, some of which are briefly explained below:

i. ***Toxicity studies***

The main toxicological assessment of a GMO deal with the protein expression studies of inserted gene(s). Another concern is the expression of novel proteins in host organisms due to genetic modification and resulting changes in the metabolism, if any. *In vitro* and *in vivo* studies are needed to assess the same using unmodified GMOs as controls. The standard toxicology methods are often well documented in the scientific and technical literature and the appropriate protocols can be drawn for each GMO.

In transgenic plant tissues, the concentration of novel protein expressed can be very low, often much less than 0.1% on dry weight basis. Studies, such as acute toxicity testing, which require relatively large amounts of material are often not feasible using the protein purified from plant tissue. Instead, these studies normally make use of protein purified from bacterial expression systems. In such cases, it is necessary to demonstrate the functional equivalence (i.e., equivalence of physicochemical properties and biological activities) of proteins purified from the two sources.

ii. ***Allergenicity***

These risks are more difficult to determine except in simple cases where the transgenes come from a species that is known to involve a risk of allergic reactions or even codes for an already identified allergen. If not, the assessment may be based on the structural similarities between the product of the transgene and known allergens and on the residual levels of the proteins coded by the transgene in the product for use/consumption. Databanks for potentially allergic peptides are available that facilitate these studies. Detailed protocols have been defined in the guidelines which may be referred to while evaluating the proposals.

As an example, in genetically modified plants the common criteria to make decisions regarding allergenicity can include:

i. whether the source of genetic material is known to contain allergens.

ii. assessment of amino acid sequence of allergens.

iii. immunoreactivity assessment.

iv. effect of pH and/or digestion since most allergens are resistant to gastric acidity and to digestive proteases
v. heat or processing stability studies

iii. ***Nutritional analysis***

Nutritional analysis is necessary particularly for GMOs to be used as food or feed. Unintended changes in level of nutrients and expression of other biochemicals can occur in many ways including through insertion of genetic material. Food safety assessments should consider the potential for any charge in nutritional composition. For genetically engineered plants aiming at altered nutritional value, the nutritional evaluation should demonstrate that there has been non intentional charges in the levels of key nutrients, natural toxicants or anti nutrients or the bioavailability of nutrients.

1.3 Environmental considerations

In addition to the effect of inserted gene(s) and their impact on genotype and phenotype of a modified organism, it is important to study the proliferation of the GMO in the environment and the effect on its equilibrium.

Environmental risk assessment of GMOs must be undertaken on a case to case basis and there can be no single method or model to follow. Broader issues include the potential adverse effects, likelihood of these risks becoming a reality, consideration of risk management strategies and assessment of overall potential environmental impact.

Possible adverse effects include outcrossing between a GMO and pathogens, negative adverse effect on population of non target organisms, including indirect effects on population levels of predators, competitors, herbivores, symbionts, parasites and pathogens.

Identification of any potential adverse effect is followed by a stage in which an estimation is made of the likelihood that the identified potential adverse effect will actually occur. It is important to estimate the chances of each of potential effect for assessment purposes.

The likelihood of certain potential adverse effects occurring can be influenced by characteristics of the size and scale of application in addition to those of inserted transgene and the recipient organism.

2. Containment facilities

In general, biosafety begins with ensuring the workplace whether it is a laboratory, fermentation plant or open fields, safe for the working staff, the general population and finally, the environment by proper containment/ confinement.

Containment covers both the research stage, when modifications are made, development work in the laboratory, greenhouse or growth room, manufacturing units where GMOs are used for production and open fields where they are released. When a new research project is initiated, it involves the modification of organisms within a laboratory under very controlled conditions. The risks involved are only perceived ones for those working in the laboratory and containment parameters are devised to ensure that the organism would not escape into the environment, or if it should, it would have been so designed not to survive in the open. At this stage, the associated risks are mainly to the human health. However, when the GMOs are used in an industrial or commercial environment, or in open cultivation, the volume of material is considerably larger and the individuals working with GMOs may be less knowledgeable or competent for handling the situation. This implies that there is possibility of accidental escape in a volume large enough for the GMO to survive and persist in the open environment. There is also a risk of accidental release where the waste from industrial unit/fields is not as carefully monitored as in the laboratory. Therefore, the containment requirements in these cases would take into account both impact on human health and possible environmental effects.

The containment could be physical, where there are real barriers to prevent escape or biological where the organism is designed not to be able to survive in any environment other than that of the laboratory. The containment facilities and biosafety practices have been defined in detail in "Recombinant DNA Safety Guidelines, 1990" of DBT. In brief, the basic laboratory guidelines have been detailed that are fundamental to all classes of risk groups followed by modifications for work with more dangerous pathogens. For more details, the most reliable reference is Laboratory Biosafety Manual of the World Health Organisation and is available at its website. A summary of recommended biosafety levels for infectious agents is given in Table 4:

It may be noted that effective physical containment of bacteria, viruses and other microbes can be extremely difficult because they cannot be seen and once disbursed cannot be recovered. Biological measures often provide better containment options in these cases. Using biological and physical containment measures in concert offer advantages to achieve a specified level of containment. It may also reduce the physical requirements to those of the next lower biosafety

Table 4: Summary of recommended Biosafety Levels for Infectious Agents

Biosafety Level	Practice and Techniques	Safety	Facilities
1.	Standard microbiological practices	Non primary containment provided by adherence to standard laboratory practices	Basic
2.	Level 1 practices plus laboratory coats; decontami nation of all infectious wastes limited access; protective gloves and biohazard warning signs as indicated	Partial containment equipment (i.e. Class I or II Biological Safety Cabinets) used to conduct mechanical and manipulative procedures that have aerosol potential that may increase the risk of exposure to personnel	Basic.
3.	Level 2 practice plus special laboratory clothing, controlled access	Partial containment equipment used for all manipulations of infectious material	Containment
4.	Level 3 practices plus entrance through change room where street clothing is removed and laboratory clothing is put on shower on exit, all wastes are decontaminated on exit from the facility	Maximum containment equipment (i.e. class III biological safety cabinet or partial containment equipment in combination with full body air supplied, positive pressure personnel suit used for all procedures and activities	Maximum containment

level. For example, an experiment design to evaluate tomato plants genetically engineered for resistance to tomato spotted wilt virus involves three organisms i.e. tomatoes, the virus and thrips, the insect vector that transmits the virus. Whereas physical containment would be provided by a greenhouse with

antivirus screening or by conducting the experiment in insect proof cages within the greenhouse, biological containment could be added by removing alternate host plants for the virus both in and outside of the greenhouse and by applying stringent insect control measures in the surrounding area.

A detailed checklist for according approval to a laboratory for carrying out recombinant DNA technology work has been given in "Recombinant DNA Safety Guidelines, 1990" of DBT. In addition to these guidelines, some of the key points as referred from WHO guidelines are given in brief below:

i. Premises and lab

- Appropriate containment: code of practice; lab design and facilities; health and medical surveillance; specification for gene technology lab; specification for large scale operations
- Prevention against entry of pests (air pressure, exhaust air, input air)
- Provisions for emergency
- Provisions for storage and disposal: In process material; starting material; finished product; infected material/rejected
- Cleanliness and hygiene
- Repair facilities

ii. Equipment

- Adequacy of equipment: appropriate design; set up and maintenance
- Standard Operating Procedures (SOPs): validation of all equipment; calibration of all instruments; investigating recording all deviations and expertise
- Automated equipment: computer controlled system; back-up file maintenance and hard copy systems

iii. Animal facilities

- Receipt of animals, including identification of person responsible and required documentation; maintenance, evaluation of health status; housing, feeding, handling; isolation of sick animals, preventive measures, treatment and quarantine for newly received animals

- Pest control system: facilities for waste, caracass; cleaning, sterilization and maintenance of supplies and equipment (animal cages, racks)

iv. Environment

- SOPs to minimize contamination: monitoring frequency; methods for viable counts in air, water, surface and non viable particulates in air.

The checklist suggested above is for standard requirements of a laboratory carrying out work in recombinant DNA technology. Appropriate reviews need to be undertaken based on the type of organisms used and the experiments planned.

3. General considerations

3.1 Status of the Organisation

It is important to make a note of the status of the organisation vis-à-vis its activities to get an idea on the capabilities to undertake the proposed research activities. In case of industry, the activities of the company or its associates in the areas other than biotechnology should also be reviewed to give an overall idea of organisation's standing and approach. In case of institutions, any affiliation to apex bodies such as CSIR, UGC, ICMR and ICAR should be noted. If it is an independent research institute, credentials should also be reviewed. The observations with regard to the status of organisation help in reviewing long-term accountability to meet statutory requirements. The indicative points are given below:

i. Constitution - university departments/Industry/ research institution/ deemed university/ private research laboratory/contract research organisations
ii. Affiliation - national bodies/CSIR/UGC/ICMR/ICAR/ major industrial groups
iii. Braches - subsidiaries organisation
iv. Major activities
v. Year of establishment
vi. Year of initiating rDNA activities
vii. Year of setting up IBSC

3.2 Organisational structure

Information regarding organisational framework such as levels of authority, chain of command, product range etc. needs to be inspected. It is necessary to ensure that supervision at various levels by senior scientists is built in the organisation structure. The number of specialists having appropriate qualifications and skills should be looked at as to whether they are in line with the complexity of the proposed projects. Necessary provisions against unauthorized entry and staff movement in restricted areas of the organisation should also be in built to ensure the compliance of the assigned risk category.

3.3. Source of funding

The sources of funding of research projects in biotechnology should also be specified by the PI and reviewed by IBSC. The funding could be from the government departments or apex bodies such as DBT, DST, UGC, CSIR, ICMR etc., industry, NGO/donor organisations, foreign bodies and their affiliation like WHO, UNIDO or any UN organisation or any foreign country as collaborative project. This helps in understanding the objective of the proposed research in terms of economic implications and benefits to the country. The information may be collected as follows:

i. Estimated project cost
ii. Estimated time for development
iii. Stage of development - basic research; lab scale development; large scale manufacture; marketing
iv. Sources of funds for development - In-house; State/Central Government (such as DBT, DSIR, MoH, MoEF); International Organisations (UNDP, UNIDO, FAO etc.) Industry; National and International NGOs/ Donors etc.

3.4 Status of other approvals required

Apart from the approval of IBSC, the rDNA activities under consideration may require approvals from other regulatory agencies such as Drug Control Authorities, Animal Ethics Committee and Plant Quarantine Authorities. Further, the status of in-house R&D recognition by organisations such as DSIR

accreditation by DST may also be reviewed. When the facilities have been set up as per the GMP/GLP specifications and have certification from reputed agencies such as WHO, ISO etc., IBSC would be able to recommend conducting experiments in higher risk categories.

3.5 Status of documentation

Inadequate familiarity with the modified organisms calls for detailed precautions while working with them. It is extremely important to document the experiments and observations in more detail than when working with common organisms. Any, unexpected effects observed in the later stages of the experiments, should be carefully documented. This would make possible to trace the experiment back and eventually come to the sources of the observed effect.

Detailed documentation also contributes to the building up of familiarity, which in future may lead to amendment of the risk safety assessment and an assignment of a lower level of containment.

3.6 Availability of trained/skilled personnel

GMOs may be used in contained laboratories or pilot plants. Alternatively, they may be used in an industrial setting or open fields. It may be noted that normally a research and development laboratory will be working with organisms, which pose a greater threat to either the individuals working therein or to the environment than those organisms, which have been developed for large scale use. The majority or organisms used in industrial production/large scale use are well characterized. On the other hand at the development stage when the modified genes are inserted into organisms, the unpredictability of insertion site requires greater care than that taken at the production facility. Organisms used in the research laboratory may be pathogenic to humans and/or harmful to the environment. Experiments could involve organisms and/or inserts, which may be injurious to the health of the workers or to those who are incidentally in the laboratory. It is therefore extremely important that the research and laboratory staff are well trained in biosafety requirements.

SUBMISSION OF APPLICATIONS TO REVIEW COMMITTEE ON GENETIC MANIPULATION (RCGM)

III

Submission of Applications to Review Committee on Genetic Manipulation (RCGM)

In the light of extensive range of activities being undertaken in recombinant research in the country and data requirements for specific stages of research and development, DBT has restructured the forms for submission of applications to Review Committee on Genetic Manipulation (RCGM). The forms have been classified into various categories and numbered accordingly. Formats for issue of approvals have also been included. The following sections provide general guidelines to the applicants for facilitating compliance and timely processing of their applications and the list of applicable forms for various activities.

1. General guidance for applicants

i. Appropriate application forms to be used by the applicant for submitting applications to IBSC & RCGM to avoid inconvenience and delays.

ii. All the applications should be signed by the applicant and countersigned by the Chairman, IBSC.

iii. Applications for consideration of RCGM to be submitted at least three weeks prior to the ensuing RCGM meeting.

iv. Applications for the conduct of confined field trials (event selection trial and BRL-I) to be submitted to Member Secretary, RCGM at least 60 days in advance of the proposed trials.

v. The applications to be submitted on A4 size paper, and the font used should be clearly legible (preferably Arial 12 may be used with at least 1" margin on the left hand side).

vi. All the dossiers including proposed protocols, preclinical study reports,

biosafety data etc to be submitted in spirally bound copies (no files of any sort to be used).

vii. All the enclosures (including dossiers) to be submitted to RCGM to be printed on both sides.

viii. All enclosed documents should be properly listed, pagenated and numbered sequentially in the same order. Annexures should be flagged.

ix. The enclosures to be numbered in continuation. If different reports bound together have different page numbers, the same may be renumbered manually to provide continuity for referring by the Members and must be properly indexed.

x. Annexures as mentioned in the form to be attached properly, (preferably using tagged) so that they are not unnoticed during circulation.

xi. GLP certificate to be submitted with the application to RCGM by the applicant in case of preclinical toxicity studies.

xii. Any figures, diagrams, pictures (such as those of gels) and photographs included in the dossier and shown in presentation slides to be clearly labeled as well as visible, preferable in colour.

xii. The units for all the values in the application form and enclosed documents to be provided

xiv. Apart from the approval of IBSC, the r-DNA activities under consideration which may require approvals from other regulatory agencies such as DGFT and Animal Ethics Committee to be mentioned.

xv. Quality assurance certificate to be submitted by the head of the institution and verified by the regulatory head of the Organisation.

xvi. The information/data to be covered in the presentation to be made to RCGM should be covered in the study reports/dossiers submitted already.

xvii. The presentations (font and colour)should be made in such a manner so that they are clearly visible upto a distance of 15 metres.

xviii. An executive summary to be made available for circulation at the time of presentation (should be attached with the application also).

xix. A soft copy of the executive summary and the dossier is to be provided in a CD(2Nos.) for record by the regulatory authorities.

2. Application forms

The category wise list of forms for various activities and stages of the development process of GMOs /LMOs is given below followed by the text of the forms. The electronic copy of the forms is provided in the enclosed CD and available at http://dbtbiosafety.nic.in and http://www.igmoris.nic.in

A. IBSC Registration and Reporting

Form A1: Application for registration of an Institutional Biosafety Committee (IBSC)

Form A2: Application for renewal of IBSC

Form A3: Annual Report of the IBSC to RCGM

Form A4: Medical Surveillance Report

Form A5: Confidentiality agreement with IBSC members including DBT nominee

B. Import, Export, Transfer and Receive

Form B1: Application to RCGM for import of GMOs/LMOs and product(s) thereof for research and development purpose.

Form B2: Permit letter for authorization to import of GMOs/LMOs and products thereof for research and development purpose

Form B3: Application to RCGM for export of GMOs/LMOs and product(s) thereof for research and development purpose.

Form B4: Permit letter for authorization to export of GMOs/LMOs and products thereof for research and development purpose

Form B5: Application to RCGM for receiving GMOs/LMOs and product(s) thereof for research and development purpose within in India.

Form B6: Permit letter for authorization to receive GMOs/ LMOs products thereof for research & develoment purpose within in India

Form B7: Application to RCGM for transfer of GMOs/LMOs and product(s) thereof for research and development purpose within India.

Form B8: Permit letter for authorization to transfer GMOs/LMOs and products thereof within India

C. Activities involving Research, Production, Preclinical Studies of GMOs in Healthcare

Form C1: Information to RCGM to carry out research involving GMOs/LMOs for development of r-DNA products for healthcare and industrial use

Form C2: Information on record taken by RCGM for research involving GMOs/ LMOs for development of rDNA products for healthcare and industrial use

Form C3: Application to RCGM to conduct preclinical and/or safety studies of rDNA products developed using GMOs/LMOs for healthcare, industrial or any other use.

Form C4: Permit for conduct of preclinical safety studies of rDNA product(s) in healthcare

Form C5: Format for submission of preclinical or other safety studies report of rDNA products developed using GMOs/LMOs for healthcare, industrial or any other use

Form C6: Recommendation of rDNA product(s) for healthcare use to DCG(I) for the appropriate phase of clinical trial

D. Activities involving Research and Safety Studies of GE Plants.

Form D1: Information to RCGM to carry out research involving GMOs/LMOs for agricultural and environmental applications

Form D2: Information on record taken by RCGM for research involving GMOs/ LMOs and development of rDNA products for agricultural and environmental applications

Form D3: Application to RCGM for approval of biosafety protocols/ studies for safety assessment of GMOs/LMOs for agricultural & environmental use.

Form D4: Permit for conduct of safety studies of GMOs/LMOs for agricultural and environmental use.

Form D5: Format for submission of safety studies of rDNA products of GMOs/LMOs for agricultural and environmental use.

A: IBSC REGISTRATION AND REPORTING

APPLICATION FOR REGISTRATION OF AN INSTITUTIONAL BIOSAFETY COMMITTEE (IBSC)

1. **Name and address of the Organisation:**

   _____

   _____

   Phone, fax & email: _____

2. **Head of the Organisation:**
   (Please provide contact details including postal address, phone, fax and e-mail)

   _____

   _____

   Phone, fax & email: _____

3. **Contact Person/(Proposed Member Secretary):**
   (Please provide contact details including postal address, phone, fax & e-mail)

   _____

   _____

   Phone, fax & email: _____

4. **Proposed activities/projects to be undertaken:**

   _____

   _____

5. **Indicate the list of organisms/genetically engineered organisms to be used:**

   _____

   _____

6. **Category of biosafety level as per the Recombinant DNA Safety Guidelines, 1990 issued by Department of Biotechnology:**

   _____

   _____

7. Containment facilities available for rDNA activities:

a. Laboratory set up

_____

_____

b. Greenhouse/nethouse (Details may include structure, size, size of the mesh etc.):

_____

_____

c. Any other specialized facility

_____

_____

8. Proposed composition of IBSC:

	Name
Chairperson	
Member Secretary	
Members (3 or more scientists engaged in rDNA molecular biology)	
Outside experts in the relevant discipline	
Medical officer/ Biosafety officer (Copies of CVs to be attached)	

9. Suggestion for suitable experts (3 nos.) working in similar area who could be identified as DBT nominee:

_____

_____

10. Please provide a brief write up about your organisation including details of infrastructural facilities available to carry out r-DNA activities in not more than 500 words:

_____

_____

_____

Date: **(Head of the Organisation)**

APPLICATION FOR FOR RENEWAL OF AN INSTITUTIONAL BIOSAFETY COMMITTEE (IBSC)

1. **Name of the Organisation:**

   _____

2. **Head of Organisation:**

   _____

3. **Complete address:**
   (Please provide contact details including postal address, phone, fax and e-mail)

   _____

   _____

4. **Date of constitution of IBSC:**
   (Please provide the copy of the O/M issued by DBT)

   _____

   _____

5. **DBT Office Memorandum No.:**

   _____

6. **Present composition of IBSC:**

	Name
Chairperson	
Member Secretary	
Members (3 or more scientists engaged in rDNA molecular biology)	
Outside experts in the relevant discipline	
Medical officer/ Biosafety officer	

7. **Number of meetings held in last three years:**

_____

8. **Whether you have submitted minutes of all the meetings held:**

Yes ☐ No ☐

9. **Brief overview of activities undertaken and GMOs handled:**

_____

10. **Proposed composition of IBSC:**

	Name
Chairperson	
Member Secretary	
Members (3 or more scientists engaged in rDNA molecular biology)	
Outside experts in the relevant discipline	
Medical officer/ Biosafety officer (Copies of CVs to be attached)	

11. **Updated status of containment facilities:**

a. Laboratory set up

_____

_____

b. Greenhouse/nethouse (Details may include structure, size, size of the mesh etc.):

_____

_____

c. Any other specialized facility

_____

_____

12. Suggestion for three suitable experts working in similar area who could be identified as DBT nominee:

_____

_____

13. Please provide a brief updated write up about your organisation including details of infrastructural facilities available to carry out rDNA activities in not more than 500 words :

_____

_____

_____

_____

FORM A3

ANNUAL REPORT OF THE INSTITUTIONAL BIOSAFETY COMMITTEE TO RCGM

1. **Name of the Organisation:**

   _____

2. **DBT Office Memorandum No.:**

   _____

3. **Date of IBSC constitution:**

   _____

4. **Composition of IBSC:**

   Chairperson: _____

   Member Secretary: _____

   DBT Nominee: _____

   Members: _____

   Outside Experts: _____

   Biosafety Officer/ Medical Officer: _____

5. **Changes in IBSC composition during the year, if any:**

   _____

6. **Details of IBSC meetings during the year:**

   a. Number of meetings held: _____

   b. Dates of each meeting: _____

   c. Whether the minutes have been sent to RCGM:

   Yes ☐ No ☐

   d. Whether the details have been posted on the http://dbtbiosafety.nic.in:

   Yes ☐ No ☐

7. **Examination & Clearance of the proposals during the period:**

S. No.	Title of the project	Principal Investigator/ Project Coordinator	Risk category as per rDNA Safety guidelines, 1990	Status of approval by IBSC and RCGM (if forwarded)

8. **Import/ Exchange of material for Research/Training:**

_____

9. **Pilot operations/confined field trials conducted during the period:**

_____

10. **Whether all projects approved by IBSC are being carried out:**

Yes ☐ No ☐

11. **Whether all projects approved by RCGM are being carried out:**

Yes ☐ No ☐

12. **Training programmes related to biosafety:**

a) Programmes conducted in-house

_____

b) Participation in national/international programmes

_____

13. **Yearly health surveillance (as applicable) conducted:**

Yes ☐ No ☐

14. **Whether the appropriate waste treatment & disposal facilities are being used in all projects to avoid risks to the environment?:**

Yes ☐ No ☐

15. Accidents, if any & emergency measures taken:

_____

_____

_____

_____

16. Any other relevant information:

_____

_____

_____

_____

Date: **(Head of the Organisation)**

MEDICAL SURVEILLANCE REPORT

1 Personal Details

i. Name of the Organisation:

_____

ii. DBT Office Memorandum No.:

_____

iii. Name of the personnel:

_____

iv. Designation

_____

v. Department: _____

Phone: _____

Email: _____

DOB: _____

2. Contact with products of rDNA Technology

Please indicate rDNA products, tissue, blood, or biological agents that you work with (tick yes or no):

i. Do you work with recombinant DNA technology? If yes, please specify

Yes ☐ No ☐

ii. What is the biosafety containment level requirement of organisms handled by you?

☐ BSL-1 ☐ BSL-I ☐ IBSL-III ☐ BSL-IV

iii. Do you work with human blood products or human tissue? If yes, please specify

Yes ☐ No ☐

iv. Do you work with animal blood products or animal tissue? If yes, please specify

Yes ☐ No ☐

3. Medical History

i. Have you had any change in your health status in the previous year? If yes, please describe

Yes ☐ No ☐

ii. Have you developed any chronic illness in the past year? If yes, please describe

Yes ☐ No ☐

iii. Have you developed any new allergies in the past year? If yes, please describe

Yes ☐ No ☐

iv. Have you been told by a physician that you have an immune compromising medical condition or are you taking medications that impair your immune system (steroids, immuniosuppressive drugs, or chemotherapy)?

Yes ☐ No ☐

4. If yes to any of the above, please attach a medical surveillance report certified and signed by the registered medical practitioner in the following format:

i. Date of health surveillance

_____

ii. Test or examinations performed and results

_____

CONFIDENTIALITY AGREEMENT WITH IBSC MEMBERS INCLUDING DBT NOMINEE

As a member of the Institutional Biosafety Committee (IBSC) constituted by the _____ (Name of Organisation) as per provisions of "Rules for the manufacture, use/import/export and storage of hazardous microorganisms/genetically engineered organisms or cells, 1989" notified by the Ministry of Environment and Forests (MoEF), Government of India under the Environment (Protection) Act, 1986.

I hereby declare that I am aware of my obligations to respect confidentiality of applications, issues and other matters placed before the IBSC and discussed thereupon, during my entire tenure of membership of IBSC. I hereby solemnly agree and undertake to maintain the confidentially of the proposals and other related information made available to me for review, reference or discussion. I hereby further agree and undertake not to divulge any confidential or Intellectual Property (IP) or commercial business information (CBI) of the organisation/institute acquired as a result of my review of such proposals and subsequent discussions arising there from. I shall also respect the confidential nature of the opinions expressed by other IBSC members or experts during discussions in meetings or provided in written form and would not divulge the same to any person, press or media.

I also agree that I would avoid any conflict of interest such as relationship with any applicant, financial interest and providing any consultancy, advice, services as an individual/scientist to any applicant except of the academic, scientific and intellectual nature.

Executed at: _____on (Date) _____

Signature :

Name & Address:

B. IMPORT, EXPORT, TRANSFER AND RECEIVE

APPLICATION TO RCGM FOR IMPORT OF GENETICALLY MODIFIED ORGANISMS (GMOs)/LIVING MODIFIED ORGANISMS (LMOs) AND PRODUCT(S) THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE

---

1. **Name of the Applicant:** _____

   Designation: _____

   Contact Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:** _____
3. **Objectives of the proposal:** _____
4. **Description of the GMOs/LMOs and product thereof (in scientific terms):**

   (a) Morphology

   _____

   (b) Physiology

   _____

   (c) Pathogenicity, if any

   _____

   (d) Number of copies of the genes incorporated

   _____

   (e) Status of approval is country of origin.

   _____

5. **Details on:**

   (a) Source of nucleic acid(s):

   _____

(b) Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene):

_____

(c) Vector(s) (Please enclose the map of the vector gene):

_____

(d) Sequence of the genes incorporated/ to be incorporated into the host organism.

_____

(e) Host(s) that carrying the vector(s)/ target gene(s):

_____

(f) Manipulative procedures used:

_____

6. Quantity of GMOs/LMOs and products thereof to be imported:
(Please specify the number and type of total packs such as vials, plates etc and the size/quantity in each pack)

_____

7. Details of earlier imports:

7.1 Whether the proposed GMOs/ LMOs and products thereof was imported earlier:

Yes ☐ No ☐

If yes, provide the copy of relevant permit issued previously and quantities imported (please specify the number of total packs such as vials, plates etc and the size in each pack and the total quantity as the case may be).

7.2 Statement of utilization on the earlier GMOs/LMOs and products thereof imported:

_____

8. Proposed work plan

8.1 Summary of the proposed work plan utilizing GMOs/LMOs and products there of: (This should indicate schematic lab work, green house or any other studies proposed to be undertaken)

_____

8.2 Category (biosafety level) of experiments to be done as per the Recombinant DNA Safety Guidelines issued by DBT: _

_____

9. Source and transport details:

9.1 Source of GMOs/LMOs and products thereof proposed to be imported:

Name of the Agency: _____

Contact person's name: _____

Address: _____

Telephone No.: _____

Fax No.: _____

e-mail: _____

9.2 Mode of Transport:

☐ Rail ☐ Road ☐ Air ☐ Ship

9.3 Safety norms to be observed during transit:

10. Proposed containment facility:
(Please indicate the level of containment proposed)

11. Proposed decontamination, disposal mechanisms & risk management measures:

12. Any other relevant information:

13. Declaration:

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Recombinant DNA Safety Guidelines" issued by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be strictly followed. The imported material will be utilized for the said purpose only. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" on its meeting held on_____ and is forwarded to RCGM for further necessary action.(copy of the minutes of relevant meeting enclosed)

Date : **Signature and Name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM , Department of Biotechnology for consideration by RCGM

2. Enclosures should include
   - Sequence map of the gene
   - Vector Map
   - Copy of the import permit, if issued earlier
   - Copy of the Utilization certificate, if imported earlier
   - Copy of the minutes of IBSC meeting in which the proposal was approved
   - Copy of the Material Transfer Agreement duly signed by both parties

PERMIT LETTER FOR AUTHORIZATION TO IMPORT OF GENETICALLY MODIFIED ORGANISMS (GMOs)/LIVING MODIFIED ORGANISMS (LMOs) AND PRODUCTS THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Permittee

Name: _____

Organisation: _____

Address: _____

Phone, fax & email: _____

Subject: _____

AUTHORISATION: In accordance with the Allocation of Business Rules 1961 of Government of India, as notified vide Notification No. CD-172/86 dated 27.02.1986 and Notification No. CD-87-87 dated 31.01.1987 and the powers conferred through the Sections 6,8 and 25 of the Environment (Protection) Act, 1986 read along with the Central Government Gazette Notification No. GSR 1037(E), dated 5.12.1989 issued by the Ministry of Environment and Forests, New Delhi and based on the recommendations of the Review Committee on Genetic Manipulation (RCGM) in its meeting held on _____, the Department of Biotechnology hereby accords authorization to (Name of the organisation) _____ to import of (Name of the product) _____ from (Name of source agency _____ for research and development purposes with properties indicated below, subject to the conditions mentioned in this letter.

PERIOD: The permit letter shall be in force from _____ to _____ unless it is sooner suspended or cancelled under the said Rules.

DESCRIPTION OF GMOs/LMOs/MATERIALS:

1. GMOs/LMOs/material(s) to be imported: _____
2. Quantities of the material(s) to be imported: _____
3. **Purpose:** _____

4. **Source of material(s) (Name, Organisation, address):** _____

_____

5. **Type of permit:**

The permission is granted for import of (Name of the GMOs/LMOs and product thereof) _____ by (Name of the organisation) _____ within a period of _____ and in a single shipment/a maximum of _____ shipments.

6. **Instructions for use:**

i. No GMOs/LMOs are allowed for experimentation for commercial production/ manufacturing of the product without prior authorization from the Competent Authority.

ii. All rDNA materials are to be destroyed and disposed of in accordance with the Recombinant DNA Safety Guidelines, 1990 of the Government of India after conclusion of the experiments.

iii. All experiments to be carried out are to be documented.

iv. The applicant is directed to submit fresh application to RCGM with the approval of IBSC for information to carry our R&D work on the _____ respectively and would submit the 'statement of utilization of the imported material to this Department

v. Any other specific instructions

7. **Condition(s) of issuance:**

8. **Mode of Transport:**

☐ Rail ☐ Road ☐ Air ☐ Ship

9. **Handling and packing instructions:**
The above _____ mentioned herein shall be handled, packaged and transported as specified in "r-DNA Safety Guidelines-1990" of the Government of India.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to:

i. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodi Road, New Delhi - 110 003

ii. The Director, NBPGR (in case of import of any planting material)

iii. M/s_____ (applicant)

iv. Office copy for file

v. Guard file

FORM B3

APPLICATION TO RCGM FOR EXPORT OF GENETICALLY MODIFIED ORGANISMS (GMOs)/LIVING MODIFIED ORGANISMS (LMOs) AND PRODUCT(S) THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE

1. **Name of the Applicant:** _____

   Designation: _____

   Contact Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:** _____

3. **Objectives of the proposal:** _____

4. **Description of the GMOs/LMOs and product thereof (in scientific terms):**

   (a) Morphology

   _____

   (b) Physiology

   _____

   (c) Pathogenicity, if any

   _____

   (d) Number of copies of the genes incorporated

   _____

5. **Details on:**

   (a) Source of nucleic acid(s):

   _____

   (b) Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene):

   _____

(c) Vector(s) (Please enclose the map of the vector gene):

_____

(d) Sequence of the genes incorporated/ to be incorporated into the host organism.

_____

(e) Host(s) that carrying the vector(s)/ target gene(s):

_____

(f) Manipulative procedures used:

_____

6. Quantity of GMOs/LMOs and products thereof to be exported:
(Please specify the number of total packs such as vials, plates etc and the size/ quantity in each pack)

7. Details of earlier exports:

7.1. Whether the proposed GMOs/ LMOs and products thereof was exported earlier:

Yes ☐ No ☐

If yes, provide the copy of relevant permit issued previously and quantities exported (please specify the number of total packs such as vials, plates etc and the size in each pack and the total quantity as the case may be).

8. Recipient & transport details:

8.1 Details of recipient where GMOs/LMOs and Products proposed to be exported:

Name of the Agency _____

Contact person's name _____

Address _____

Telephone No. _____

Fax No. _____

e-mail _____

8.2 Mode of Transport:
☐ Rail ☐ Road ☐ Air ☐ Ship

8.3 Safety norms to be observed during transit:

9. Any other relevant information:

10. Declaration:

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Recombinant DNA Safety Guidelines" issued by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be strictly followed. The exported material will be utilized for the said purpose only. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.(copy of the minutes of relevant meeting enclosed)

Date : **Signature and Name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosures should include:
   - Sequence map of the gene
   - Vector Map
   - Copy of the export permit, if issued earlier
   - Copy of the minutes of IBSC meeting in which the proposal was approved
   - Copy of the Material Transfer Agreement duly signed by both parties

PERMIT LETTER FOR AUTHORIZATION TO EXPORT OF GENETICALLY MODIFIED ORGANISMS (GMOs)/LIVING MODIFIED ORGANISMS (LMOs) AND PRODUCTS THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Permittee

Name: _____

Organisation: _____

Address: _____

Phone, fax & email: _____

Subject: _____

AUTHORISATION: This is in response to your letter No. _____ dated _____ on the above mentioned subject. It is informed that your application was considered by the Review Committee on genetic Manipulation (RCGM) in its meeting held on _____. RCGM noted the objectives of the proposal and expressed that the committee has no objection for export of (Name of the product) _____ to M/s. (Name of the recipient organisation) _____ .

PERIOD: The permit letter shall be in force from ____ to ____ unless it is sooner suspended or cancelled under the said Rules.

DESCRIPTION OF GMOs/LMOs/MATERIALS:

1. **GMOs/LMOs/Material(s) to be exported:** _____
2. **Quantities of the material(s) to be exported in terms of number of total packs such as vials, plates etc and the size/quantity in each pack etc.:** _____
3. **Purpose:** _____

_____

4. **Export to:** _____

   Name of Organisation: _____

   Address: _____

   Phone, fax & e-mail: _____

5. **Type of permit:**

   The permission is granted for export of (Name of the GMOs/LMOs and product thereof) _____ by (Name of the organisation) _____ within a period of _____ and in a single shipment/ a maximum of _____ shipments.

6. **Condition(s) of issuance, if any, specified by RCGM:**

7. **Mode of Transport:**

   ☐ Rail ☐ Road ☐ Air ☐ Ship

8. **Handling and packing instructions:**

   The above _____ mentioned herein shall be handled, packaged and transported as specified in "r-DNA Safety Guidelines-1990" of the Department of Biotechnology, Government of India.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to:

i. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodi Road, New Delhi - 110 003

ii. National Biodiversity Authority (as the case may be)

iii. M/s_____ (applicant)

iv. Office copy for file.

v. Guard file

APPLICATION TO RCGM FOR RECEIVING GENETICALLY MODIFIED ORGANISMS (GMOs)/LIVING MODIFIED ORGANISMS (LMOs) AND PRODUCT(S) THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE WITHIN INDIA

---

1. **Name of the Applicant:** _____

   Designation: _____

   Contact Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:** _____

3. **Objectives of the proposal:** _____

4. **Description of the GMOs/LMOs and product thereof (in scientific terms):**

   (a) Morphology

   _____

   (b) Physiology

   _____

   (c) Pathogenicity, if any

   _____

   (d) Number of copies of the genes incorporated

   _____

   (e) Status of approval is country of origin.

   _____

5. **Details on:**

   (a) Source of nucleic acid(s):

   _____

(b) Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene):

_____

(c) Vector(s) (Please enclose the map of the vector gene):

_____

(d) Sequence of the genes incorporated/ to be incorporated into the host organism.

_____

(e) Host(s) that carrying the vector(s)/ target gene(s):

_____

(f) Manipulative procedures used:

_____

6. Quantity of GMOs/LMOs and products thereof to be received:
(Please specify the number of total packs such as vials, plates etc and the size/ quantity in each pack)

7. Details of earlier received GMOs/LMOs & products thereof

7.1 Whether the proposed GMOs/ LMOs and products thereof was received earlier:
Yes ☐ No ☐

If yes, provide the date of relevant permit issued previously and quantities received (please specify the number of total packs such as vials, plates etc and the size in each pack and the total quantity as the case may be).

7.2 Statement of utilization on the earlier GMOs/LMOs and products thereof received:

8. Proposed work plan

8.1 Summary of the proposed work plan utilizing GMOs/LMOs and products there of: (This should indicate schematic lab work, green house or any other studies proposed to be undertaken)

8.2 Category (Biosafety level) of experiments to be done as per the Recombinant DNA safety Guidelines issued by DBT:

9. **Source & transport details**

9.1 Source of GMOs/LMOs and products thereof proposed to be received from:

Name of the Organisation/Agency

Contact person's name

Address

Telephone No.

Fax No.

e-mail

9.2 Mode of Transport:

☐ Rail ☐ Road ☐ Air ☐ Ship

10. **Proposed containment facility:**
(Please indicate the level of containment proposed)

11. **Proposed decontamination, disposal mechanisms & risk management measures:**

12. **Any other relevant information:**

13. **Declaration:**
I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Recombinant DNA Safety Guidelines" issued by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be strictly followed. The recieved material will be utilized for the said purpose only. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:
The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.(copy of the minutes of relevant meeting enclosed)

Date : **Signature and Name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM
2. Enclosures should include:
    - Sequence map of the gene
    - Vector Map
    - Copy of the permit for receiving, if issued earlier
    - Copy of the statement of utilization of the earlier received GMOs/LMOs and product(s) thereof, if any.
    - Copy of the minutes of IBSC meeting in which the proposal was approved
    - Concurrence of IBSC of source organisation supplying the material
    - Copy of the Material Transfer Agreement duly signed by both parties

PERMIT LETTER FOR AUTHORIZATION TO RECEIVE GENETICALLY MODIFIED ORGANISMS (GMOs)/LIVING MODIFIED ORGANISMS (LMOs) PRODUCTS THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE WITHIN INDIA

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Name: _____

Organisation: _____

Address: _____

Phone, fax & email: _____

Subject:

AUTHORISATION: In accordance with the Allocation of Business Rules 1961 of Government of India, as notified vide Notification No. CD-172/86 dated 27.02.1986 and Notification No. CD-87-87 dated 31.01.1987 and the powers conferred through the Sections 6, 8 and 25 of the Environment (Protection) Act, 1986 read along with the Central Government Gazette Notification No. GSR 1037(E), dated 5.12.1989 issued by the Ministry of Environment and Forests, New Delhi and based on the recommendations of the Review Committee on Genetic Manipulation (RCGM) in its meeting held on _____, the Department of Biotechnology hereby accords authorization to (Name of organisation) _____ to receive of (Name of product) _____ from (Name of source agency)_____ for research and development purposes with properties indicated below, subject to the conditions mentioned in this letter.

PERIOD: The permit letter shall be in force from ____ to ____ unless it is sooner suspended or cancelled under the said Rules.

DESCRIPTION OF GMOs/LMOs/MATERIALS:

1. **GMOs/LMOs/Material(s) to be received:** _____
2. **Quantities to be received:** _____
3. **Purpose:** _____
4. **Permittee:** _____

Name: _____

Organisation: _____

Address: _____

Phone, fax & e-mail: _____

5. Source of GMOs/LMOs/material(s):

Name: _____

Organisation: _____

Address: _____

Phone, fax & e-mail: _____

6. Type of permit:

The permission is granted for receiving of (Name of the GMOs/LMOs and product thereof) _____ by (Name of the organisation) _____ within a period of _____ and in a single shipment/ a maximum of _____ shipments.

7. Instructions for use:

i. No GMOs/LMOs/material(s) are allowed for experimentation for commercial production/manufacturing of the product without prior authorization from the Competent Authority.

ii. All rDNA materials are to be destroyed and disposed of in accordance with the Recombinant DNA Safety Guidelines of the Government after conclusion of the experiments.

iii. All experiments to be carried out are to be documented.

iv. The applicant is directed to submit fresh application to RCGM with the approval of IBSC for information to carry our R&D work on the ___ respectively and would submit the 'utilization report' of the received ____ to this Department

v. Any other specific instructions

8. Condition(s) of issuance:

9. Handling and packing instructions:

The above _____ mentioned herein shall be handled, packaged and transported as specified in "r-DNA Safety Guidelines-1990" of the Government of India.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to:

i. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodi Road, New Delhi - 110 003

ii. The Director, NBPGR (in case to recieve any planting material)

iii. M/s_____ (Applicant)

iv. Office copy for file

v. Guard file

FORM B7

APPLICATION TO RCGM FOR TRANSFER OF GMOs/ LMOs AND PRODUCT(S) THEREOF FOR RESEARCH AND DEVELOPMENT PURPOSE WITHIN INDIA

1. **Name of the Applicant:** _____

   Designation: _____

   Contact Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:** _____

3. **Objectives of the proposal:** _____

4. **Description of the GMOs/LMOs and product thereof (in scientific terms):**

   (a) Morphology

   _____

   (b) Physiology

   _____

   (c) Pathogenicity, if any

   _____

   (d) Number of copies of the genes incorporated

   _____

   (e) Status of approval is country of origin.

   _____

5. **Details on:**

   (a) Source of nucleic acid(s):

   _____

(b) Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene):

_____

(c) Vector(s) (Please enclose the map of the vector gene):

_____

(d) Sequence of the genes incorporated/ to be incorporated into the host organism.

_____

(e) Host(s) that carrying the vector(s)/ target gene(s):

_____

(f) Manipulative procedures used:

_____

6. Quantity of GMOs/LMOs and products thereof to be transfered:
(Please specify the number of total packs such as vials, plates etc and the size/ quantity in each pack)

7. Details of earlier transfered GMOs/LMOs

7.1 Whether the proposed GMOs/ LMOs and products thereof was transfered earlier:

Yes ☐ No ☐

If yes, provide the copy of relevant permit issued previously and quantities transfered (please specify the number of total packs such as vials, plates etc and the size in each pack and the total quantity as the case may be).

8. Proposed work plan

8.1 Summary of the proposed work plan utilizing GMOs/ products there of: (This should indicate schematic lab work, green house or any other studies proposed to be undertaken)

8.2 Category (Biosafety level) of experiments to be done as per the Recombinant DNA safety Guidelines issued by DBT:

9. Source & transport details

9.1 GMOs/LMOs and products thereof proposed to be transferred to:

Name of the Organisation/Agency: _____

Contact person's name: _____

Address: _____

Telephone: _____

Fax: _____

e-mail: _____

9.2 Mode of Transport:

☐ Rail ☐ Road ☐ Air ☐ Ship

9.3 Safety norms to be observed during transit:

10. Containment facility required:

11. Proposed decontamination, disposal mechanisms & risk management measures:

12. Any other relevant Information:

13. Declaration:

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Recombinant DNA Safety Guidelines" issued by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be strictly followed. The imported material will be utilized for the said purpose only. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.(copy of the minutes of relevant meeting enclosed)

Date : **Signature and Name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosures should include
    - Sequence map of the gene
    - Vector Map
    - Copy of the permit, if issued earlier
    - Copy of the minutes of IBSC meeting in which the proposal was approved
    - Copy of the Material Transfer Agreement duly signed by both parties
    - Concurrence of IBSC of source organisation supplying the material

FORM B8

PERMIT LETTER FOR AUTHORIZATION TO TRANSFER GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) AND PRODUCTS THEREOF WITHIN INDIA

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Name: _____

Organisation: _____

Address: _____

Phone, fax & email: _____

Subject:

AUTHORISATION: In accordance with the Allocation of Business Rules 1961 of Government of India, as notified vide Notification No. CD-172/86 dated 27.02.1986 and Notification No. CD-87-87 dated 31.01.1987 and the powers conferred through the Sections 6,8 and 25 of the Environment (Protection) Act, 1986 read along with the Central Government Gazette Notification No. GSR 1037(E), dated 5.12.1989 issued by the Ministry of Environment and Forests, New Delhi and based on the recommendations of the Review Committee on Genetic Manipulation (RCGM) in its meeting held on _____, the Department of Biotechnology hereby accords authorization to (Name of organisation) _____ to transfer of (Name of product) _____ from (Name of source agency) _____ for research and development purposes with properties indicated below, subject to the conditions mentioned in this letter.

PERIOD: The permit letter shall be in force from _____ to _____ unless it is sooner suspended or cancelled under the said Rules.

DESCRIPTION OF GMOs/LMOs/MATERIALS:

1. **GMOs/LMOs/Material(s) to be transferred:** _____
2. **Quantities of the material(s) to be transferred:** _____
3. **Purpose:** _____
4. **GMOs/LMOs/Material(s) transferred to:** _____

Name: _____

Organisation: _____

Address: _____

Phone, fax & e-mail: _____

5. **Type of permit:**

   The permission is granted for transfer of (Name of the GMOs/LMOs and product thereof) _____ by (Name of the organisation) _____ within a period of _____ and in a single shipment/ a maximum of _____ shipments.

6. **Condition(s) of issuance:**

7. **Mode of transport:**

   ☐ Rail ☐ Road ☐ Air ☐ Ship

8. **Handling and packing instructions:**
   The above _____ mentioned herein shall be handled, packaged and transported as specified in "r-DNA Safety Guidelines-1990" of the Government of India.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to:

i. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodi Road, New Delhi - 110 003

ii. M/s_____ (applicant)

iii. Office copy for file

iv. Guard file

C. ACTIVITIES INVOLVING RESEARCH, PRODUCTION, PRECLINICAL STUDIES OF GMOs/ LMOs IN HEALTHCARE

INFORMATION TO RCGM TO CARRY OUT RESEARCH INVOLVING GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR DEVELOPMENT OF rDNA PRODUCTS FOR HEALTHCARE AND INDUSTRIAL USE

1. Name of the Applicant:

   Designation: _____

   Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. DBT Office Memorandum No.: _____

3. **Application for :** _____

   3.1 Purpose: (not more than 100 words)

   _____

   3.2 New

   Yes ☐ No ☐

   3.3 Ongoing Project

   Yes ☐ No ☐

   If yes, No. & Date of permission letter issued :

   3.4 Category (Biosafety level) of experiments as per the Recombinant DNA safety Guidelines, 1990 issued by DBT

4. **Description of the GMOs/LMOs proposed to employed in the research proposal:** (in scientific terms; for new application only)

   4.1 Description of GMOs/LMOs

   4.2 Description of the target gene(s)

   4.3 Number of copies of the genes incorporated

   4.4 Description of the target product(s)

5.Details on :

5.1 Source of nucleic acid(s) :

_____

5.2 Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene) :

_____

5.3 Vector(s) (Please enclose the map of the vector gene) :

_____

5.4 Host(s) that carrying the vector(s)/ target gene(s) :

_____

5.5 Manipulative procedures :

_____

5.6 Anticipated functions of product(s)

_____

6. Summary of the proposed work plan utilizing GMOs:
(please check it from the following areas and provide the details of work plan).

6.1 Basic transformation and laboratory work to assess the expression of the target gene _____

6.2 Standardization of fermentation/production procedures _____

7. Site/ Location of the research work :

_____

8. Proposed containment facility (Please indicate the level of containment proposed):

_____

9. Decontamination and disposal mechanisms:

_____

10. Risk management (Emergency plan):

_____

11. Any other relevant information:

_____

12. Declaration :

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Safety Guidelines" brought out by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be and is being strictly followed. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.

Date: **Signature and name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosed: (Kindly tick the enclosures)
   - Sequence map of the gene
   - Vector Map
   - Copy of the permit, if issued earlier
   - Copy of the minutes of IBSC meeting in which the proposal was approved

FORM C2

INFORMATION ON RECORD TAKEN BY RCGM FOR RESEARCH INVOLVING GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR DEVELOPMENT OF rDNA PRODUCTS FOR HEALTHCARE AND INDUSTRIAL USE

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Applicant: _____

Name of Organisation: _____

Address: _____

Phone, fax & e-mail: _____

Subject: Information submitted vide letter No. _____ dated _____

1. This is to inform that the application to Review Committee on Genetic Manipulation (RCGM) on the following projects was considered and noted by the RCGM in its meeting held on _____.

   i) _____

   ii) _____

2. Additional information sought by RCGM, if any should be separately included.
3. You are required to comply with the r-DNA Safety Guidelines-1990 of DBT.
4. Please provide the information on the above projects for updation on http://www.igmoris.nic.in as per details on the website

(Member Secretary, RCGM)

APPLICATION TO RCGM TO CONDUCT PRECLINICAL AND/OR SAFETY STUDIES OF rDNA PRODUCTS DEVELOPED USING GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR HEALTHCARE, INDUSTRIAL OR ANY OTHER USE

1. **Name of the Applicant:** _____

   Designation: _____

   Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:**

   _____

3. **Application for :**

   _____

   3.1 Purpose (not more than 100 words)

   3.2 New

   Yes ☐ No ☐

   3.3 Ongoing Project

   Yes ☐ No ☐

   If yes, No. & Date of permission letter issued and also briefly state the purpose for which permission was granted.

   3.4 Category (Biosafety level) of experiments as per the Guidelines of DBT

4. **Objectives of the proposal:**

5. **Background about the nature of the product with appropriate references:**
   (may include in about 100 words, the process of development, mode of action, therapeutic indication, therapeutic dose if available, whether product is already in use elsewhere, if yes, any known side effects, animal toxicology data, similarity / dissimilarity between the molecule / compound under consideration)

6. Molecular biology details of the GMOs/LMOs employed:

6.1 Origin of gene

6.2 Sequence

6.3 Vector/promoter/terminator

6.4 Transformation process

6.5 Host organism characteristics

6.6 Safety of the organism

6.7 Copy number of the plasmid

6.8 Stability data of the plasmid

6.9 Expression level in the host

6.10 Containment levels and biosafety

7. Standardization of fermentation/production procedures:

7.1 Basic transformation and laboratory work to assess the expression of the target gene

7.2 Five batches of reproducible fermentation data (Batch size adequate to give after purification enough purified product to generate preclinical data) with detail kinetics of one single batch.

7.3 Fermentation kinetics data from one representative batch indicating cell growth, product formation, pH, temperature, dissolved oxygen, major nutrient consumption pattern, RPM for agitation

7.4 Concentration of product/L, yield and volumetric productivity.
(Provide details to show that the specific protein yield (amount of protein per unit cell mass) remains more or less constant at different cell concentration during fermentation).

8. Downstream process for purification:

8.1 Steps involved in purification of the product

8.2 Batch size for protein purification

8.3 Description of each unit operation step during purification and recovery of protein

8.4 Quality of the product and recovery efficiency

8.5 Overall recovery of the product in each batch operation

8.6 Consistency of recovery in 5 consecutive batches of purification

9. Product/protein characterization:

9.1 Molecular weight / western blot/SDS-PAGE/ mass spec

9.2 Amino acid sequence (10 N terminal AA)

9.3 Peptic digest

9.4 Secondary structure by CD (near and far UV)

9.5 Fluorescence spectra

9.6 Disulfide bond presence if any

9.7 Carbohydrate content and details of components (for glycoproteins)

9.8 Presence of aggregates

9.9 Host cell protein/contaminants

9.10 Residual DNA and LPS/endotoxin

9.11 Pyrogen content

10. Formulation and stability studies:

10.1 Extended stability

10.2 Use of stabilizer(s) and its concentration

10.3 Product quality in formulated condition

10.4 Bioactivity/immunogenicity of the formulated product

11. Efficacy of the product: Information on:

11.1 Receptor binding assay if any

11.2 Cellular proliferation assay

11.3 Signal transduction pathways

11.4 Tissue specific activity

11.5 In vivo studies in animal models

11.6 Pharmacokinetics and Pharmacodynamics studies

12. Immunogenicity studies:

12.1 Sequence specific

12.2 Non-Specific to other proteins

12.3 Immunogenicity with adjuvants

13. Acceptability criteria of the bulk and the formulated material wherever ready for preclinical or safety studies:

14. Proposed work plan for preclinical or other safety studies:

14.1 List of the studies to be done

14.2 Information about the route of administration, dose, vehicle, mode of administra
tion in each study

14.3 Basis of dose calculation for each animal used (indicate the guidelines followed such as Schedule-Y, ICH, FDA or justify deviations if any).

14.4 Toxicity and allergenicity protocols
(Provide complete study design including test species, age, body weight, control groups such as vehicle control, comparator group, recovery groups, details of biochemical, histopathological and other parameters to be measured, organs to be weight, monitoring schedule etc.)

14.5 Address and accreditation status of the labs where studies proposed to be onducted.

14.6 Status of Institutional Animal Ethics Committee's Approval (Please specify the studies and products to be tested in each lab).

15. Proposed containment facility as well as measures:

16. Decontamination and disposal mechanisms:

17. Risk management (Emergency plan):

18. Any other relevant information:

19. Declaration :

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Safety Guidelines" brought out by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be and is being strictly followed. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be informed immediately.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.

Date: **Signature and name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosed: (Kindly tick the enclosures):
   - Sequence map of the gene
   - Vector Map
   - Copy of the import/receive permits, or any other approval letters issued earlier
   - Copy of the minutes of IBSC meeting in which the proposal was approved

FORM C4

PERMIT FOR CONDUCT OF PRECLINICAL SAFETY STUDIES OF rDNA PRODUCT(S) IN HEALTHCARE

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Permittee: _____

Name of Organisation: _____

Address: _____

Phone, fax & e-mail: _____

Subject:

AUTHORISATION: This is in response to your letter No. _____ dated _____ on the above mentioned subject. It is informed that your application was considered by the Review Committee on Genetic Manipulation (RCGM) in its meeting held on _____. On the basis of the recommendations of the RCGM and comments of the experts on the dossier, you are allowed to conduct pre-clinical safety studies on_____ on the premises located at_____, subject to the acceptance of the following terms and conditions:

a) There would be no change in the protocols approved by RCGM which includes :

_____

_____

_____

_____

_____

You would follow the protocols as per the Schedule "Y" of the Drugs and Cosmetics Act of 1940 and Rules-1945 of the Govt. of India.

b) The route of administration of the product in lab animals would be the same as of therapeutic route of administration and any other route specified in the protocols.

c) You would conduct laboratory studies with proper controls and reference materials.

d) You are also directed to include a control group of animals by taking innovator's product as gold standard in toxicity studies for comparison as per the Schedule "Y" of the Drugs and Cosmetics Act of 1940 and Rules-1945 of the Govt. of India.

e) You would be using the protocols in terms of dose fixation as was submitted to the RCGM Secretariat.

f) You would use the formulated material of in these studies as far as equivalent to the final product to be used commercially at later stage. You would maintain sufficient stocks of the formulated materials as reference inventory in proper storage conditions with the batch details of such stocks, which would be provided by you to the Competent Authority before starting the experiments as well as after completion of the studies. There would not be any subsequent major modifications or changes in the composition of the formulated material utilized in toxicology studies in animals after finalization of studies. In case of any subsequent change, the production methods or the quality of the bulk as well as the formulated material, it is to be brought to the notice of the Competent Authority and no such altered materials be used by you for commercial purpose or other wise without prior approval from the Statutory and Competent Authority.

g) You would ascertain and maintain that only Organisation's authorized personnel would be allowed to visit the experimental lab and the details of personnel visiting the lab. with dates, purpose(s) etc. would be maintained in register, which may be available for inspection, whenever required by the Competent Authority.

h) You would inform the RCGM through your Institutional Biosafety Committee (IBSC) the progress of work from time to time. The IBSC will collect all the information on experiments and would submit the consolidated information/data/ results on experiments to the RCGM once in a year.

i) You would adhere to the Recombinant DNA Safety Guidelines, 1990 and also follow the other Guidelines for generating pre-clinical and clinical data for r-DNA based vaccines, diagnostics and other biologicals brought out by the Department of Biotechnology, the Government of India, from time to time. Accidents, if any, arising out of the experiments would be brought to the notice of the Govt. immediately.

j) You are required to confirm the acceptance of the above conditions to the DBT at your earliest convenience before starting the toxicity studies. You are further informed that you may contact the Department of Biotechnology for any clarification in the matter, which you may require.

PERIOD: The permit letter shall be in force from ____ to ____ unless it is sooner suspended or cancelled under the said Rules.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to:

1. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodhi Road, New Delhi-110 003
2. The Secretary, Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi 1.
3. The Drugs Controller General of India, FDA Bhawan, Kotla Road, New Delhi - 110 002.
4. The Director General, Indian Council of Medical Research, Ansari Nagar, Post Box No.4911, New Delhi - 110 029.
5. Office copy for file
6. Guard File

FORMAT FOR SUBMISSION OF PRECLINICAL OR OTHER SAFETY STUDIES REPORT OF rDNA PRODUCTS DEVELOPED USING GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR HEALTHCARE, INDUSTRIAL OR ANY OTHER USE

1. **Name of the Applicant**: _____

   Designation: _____

   Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:** _____

3. **Objectives of the proposal:** _____

4. **Summary of the products characteristics and process of development:**

   _____

5. **List of preclinical study protocols approved by RCGM:**
   (please attach a copy of the approval letter)

   _____

6. **Preclinical study reports:**

   6.1 List of studies completed and deviations, if any from the approved protocols

   6.2 Dose calculation for conduct of safety studies

   6.3 Study reports (Each study report would reflect all the issues approved in the protocols). In addition the following to be included:

   - RCGM approval of protocol
   - IBSC approval of report
   - IAEC approval for animal use and for the procedures

- Quality assurance statement
- Signatures of study director and all investigators who were involved in the study
- All quality analytical reports on the test material and vehicle
- Animal feed and animal health certifications
- Protocol deviations if any
- Discussion on the results
- Individual animal data, summary data and any other data like computer analysis outputs etc
- Conclusion

6.4 Address and accreditation status of the labs where these studies were conducted.

7. **Measures taken for containment:**

8. **Decontamination and disposal mechanisms:**

9. **Risk management (Emergency plan):**

10. **Any other relevant information:**

11. **Declaration:**
I declare that the information provided in the above format is correct and accurate to the best of my knowledge.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.

Date: **Signature and name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosures should include
    - Copies of earlier approvals from RCGM
    - Copy of the minutes of IBSC meeting in which the proposal was approved

FORM C6

RECOMMENDATION OF rDNA PRODUCT(S) FOR HEALTHCARE USE TO DCG(I) FOR THE APPROPRIATE PHASE OF CLINICAL TRIAL

PERMIT NUMBER: **DATE OF ISSUE: _____**

To

The Drug Controller General of India,
C.H.E.B.Campus, FDA Bhawan,
Kotla Road, New Delhi - 110 002.

Subject:

M/s._____, was granted permission vide letter dated _____ to conduct preclinical safety studies on _____on the premises located at_____. It is informed that reports on pre clinical safety studies on _____ were evaluated by the Review Committee on Genetic Manipulation (RCGM) in its meeting held on _____.

Based on the submissions made by the applicant and the recommendations of the RCGM, the applicant has been directed to approach your office for approval to conduct appropriate Phase of human clinical trials on _____ by submitting all relevant information.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to:

i. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodi Road, New Delhi - 110 003

ii. M/s_____ (applicant)

iii. Office copy for file

iv. Guard file

D. ACTIVITIES INVOLVING RESEARCH AND SAFETY STUDIES OF GE PLANTS

INFORMATION TO RCGM TO CARRY OUT RESEARCH INVOLVING GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR AGRICULTURAL ENVIRONMENTAL

1. Name of the Applicant: _____

   Designation: _____

   Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:**

3. **Application for :**

   3.1 Purpose

   3.2 New

   Yes ☐ No ☐

   3.3 Ongoing Project

   Yes ☐ No ☐

   If yes, no. & date of earlier permits/letters issued:

   3.4 If yes, briefly state the purpose for which permission was granted.

   3.5 Category of experiments as per the Recombinant DNA Safety Guidelines, 1990 and/or Revised Guidelines for Research in Transgenic Plants, 1998.

4. **Objectives of the proposal:**

5. **Description of the genetically engineered organisms (including plants and animals) employed in the research proposal:**

   5.1 Description of genetically engineered organisms

   5.2 Anticipated new characters in genetically engineered organisms/ Expected difference as compared to non-transgenic counterparts.

5.3 Description of the target gene and mode of action.

5.4 Description of the other genes inserted if, any (Such as marker/ reporter gene)

5.5 History of use including toxicity and allergenicity aspects

6. Details on (Nucleic acid(s) & Vectors):

6.1 Source of nucleic acid(s) :

6.2 Copy number of gene(s) :

6.3 Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene) :

6.4 Vector(s) description (please enclose the Plasmid map) :

7. Summary of the proposed work plan:

7.1 Basic transformation work and tissue culture procedure at laboratory level and standardize the procedure to assess the expression of the target gene in the transformed material.

7.2 Transfer of target gene imported/ indigenously isolated in Indian germplasm and to assess the expression of the target gene in the transformed material.

7.3 Transfer of target gene from imported materials such as seeds to indigenous species (by backcrossing) and to assess the expression of the target gene in the transformed material.

7.4 Lab/greenhouse/nethouse/contained facility experiments on GMOs/LMOs for testing/ assessing the efficacy of their new characters.

8. Indicate whether gene is toxic to animals:

9. Indicate whether gene is allergenic to animals:

10. Geographical origin of plant:

11. Decontamination and disposal mechanisms:

12. Risk management (Emergency plan):

13. Any other relevant information:

14. Declaration:

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Recombinant DNA Safety Guidelines 1990 and Revised Guidelines for research in transgenic plants & Guidelines for Toxicity and Allergenicity Evaluation of transgenic seeds, plants and plant parts" 1998 brought out by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be and is being strictly followed. The imported material will be and is being utilized for the said purpose only. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be immediately informed.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.

Date: **Signature and Name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosed: (Kindly tick the enclosures)
    - Sequence map of the gene
    - Vector Map
    - Copy of the permit, if issued earlier
    - Copy of the minutes of IBSC meeting in which the proposal was approved

FORM D2

INFORMATION ON RECORD TAKEN BY RCGM FOR RESEARCH INVOLVING GMOS/LMOS AND DEVELOPMENT OF RDNA PRODUCTS FOR AGRICULTURAL AND ENVIRONMENTAL APPLICATIONS

PERMIT NUMBER: **DATE OF ISSUE:** _____

Permittee: _____

Name of Organisation: _____

Address: _____

Phone, fax & e-mail: _____

Subject: Information submitted vide letter _____ dated _____

1. This is to inform that the application to Review Committee on Genetic Manipulation (RCGM) on the following projects was considered and noted by the RCGM in its meeting held on _____.

   i) _____

   ii) _____

2. You are required to comply with the r-DNA Safety Guidelines-1990 of DBT and Guidelines for research in transgenic plants, 1998, as applicable while carrying out experiments in contained facility/laboratory/greenhouse/nethouse of the R&D centre.
3. Please provide the information on the above projects for updation on http://www.igmoris.nic.in as per details on the website

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

APPLICATION TO RCGM FOR APPROVAL OF BIOSAFETY PROTOCOLS/ STUDIES FOR SAFETY ASSESSMENT OF GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR AGRICULTURAL AND ENVIRONMENTAL USE

1. **Name of the Applicant:** _____

   Designation: _____

   Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:**
3. **Application for :**

   3.1 Purpose

   3.2 New

   Yes ☐ No ☐

   3.3 Ongoing Project

   Yes ☐ No ☐

   If yes, No. & Date of permission letter issued and also briefly state the purpose for which permission was granted.

   3.4 Category (Biosafety level) of experiments as per the Guidelines of DBT.

4. **Objectives of the proposal:**
5. **Description of the GMOs/LMOs (including plants and animals) in scientific terms:**

   5.1 Description of GMOs/LMOs

   5.2 Anticipated new characters compared to non-transgenic counterparts.

   5.3 Description of the target gene and mode of action.

   5.4 Source of nucleic acid(s):

5.5 Copy number of gene(s):

5.6 Nucleic acid sequence (Please enclose the nucleic acid sequence map of the target gene) :

5.7 Vector(s) description (please enclose the Plasmid map) :

6. Work completed so far: (please check it from the following areas and provide the detailed work plan).

6.1 Transfer of target gene imported/ indigenously isolated in Indian germplasm and to assess the expression of the target gene in the transformed material.

6.2 Transfer of target gene from imported seed materials to indigenous species (by backcrossing) and to assess the expression of the target gene in the transformed material.

6.3 Lab/contained facilities/greenhouse/nethouse experiments conducted so far for testing/ assessing the efficacy of their new characters.

6.4 Confined field trials conducted so far and data recorded so far (please specify whether event selection trial/biosafety research trials/any other)

6.5 Proposed work plan for safety assessment

a) Description of the material to be used for testing (including type, quantity, dos age).

b) Biochemical characterization of the material in terms of near equivalence to its non-transgenic counterpart.

c) Information on quantity of target gene product (in different parts in case of large organisms such as plant or animals) and/or at different stages of development.

d) Toxicity and allergenicity protocols for food and feed safety assessment including choices of animals route of administration, Institutional Animal Ethics Approval Committee, in case of animals studies.

e) Addresses and their accreditation status of the lab where these studies are proposed to be conducted

f) Environmental safety assessment protocols

7. Decontamination and disposal mechanisms:

8. Risk management (Emergency plan):

9. **Any other relevant information:**

10. **Declaration:**

I declare that the information provided in the above format is correct and accurate to the best of my knowledge. The "Recombinant DNA Safety Guidelines 1990 and Revised Guide1ines for research in transgenic plants & Guidelines for Toxicity and Allergenicity Evaluation of transgenic seeds, plants and plant parts" 1998 brought out by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India will be and is being strictly followed. The imported material will be and is being utilized for the said purpose only. In case any untoward incident occurs, the Chairman of the IBSC and the Member-Secretary of the RCGM will be immediately informed.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" on _____ and is forwarded to RCGM for further necessary action.

Date: **Signature of the Chairman, IBSC**

Note: Please submits 23 copies of the application to the Department of Biotechnology for placing the same in the meeting of RCGM)

Enclosed: (Kindly tick the enclosures)

- Copy of the permit, if issued earlier
- Copy of the minutes of IBSC meeting in which the proposal was approved

FORM D4

PERMIT FOR CONDUCT OF SAFETY STUDIES OF GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR AGRICULTURAL AND ENVIRONMENTAL USE

PERMIT NUMBER: **DATE OF ISSUE:** _____

DATE OF EXPIRY: _____

Permittee: _____

Name of Organisation: _____

Address: _____

Phone, fax & e-mail: _____

Subject:

AUTHORISATION: This is in response to your letter No. _____ dated _____ on the above mentioned subject. It is informed that your application was considered by the Review Committee on Genetic Manipulation (RCGM) in its meeting held on _____. On the basis of the recommendations of the RCGM, you are permitted to conduct safety studies on _____ in the premises located at_____, subject to the acceptance of the following terms and conditions:

a) There would be no change in the protocols approved by RCGM which includes:

_____

_____

_____

You would follow the guidelines issues by the Department of Biotechnology.

b) You would conduct laboratory studies with proper controls and reference materials.

c) You would be using the protocols in terms of dose fixation as was submitted to the RCGM Secretariat.

d) You would use the material of _____ in these studies as far as equivalent to the final product to be used commercially at later

stage and maintain sufficient stocks of the materials as reference inventory in proper storage conditions with the batch details of such stocks, which would be provided by you to the Competent Authority before starting the experiments as well as after completion of the studies. There would not be any subsequent major modifications or changes in material utilized in safety studies after finalization of studies. In case of any subsequent change, it is to be brought to the notice of the Competent Authority and no such altered materials be used by you for commercial purpose or other wise without prior approval from the Statutory and Competent Authority.

e) You would ascertain and maintain that only Organisation's authorized personnel would be allowed to visit the experimental lab and the details of personnel visiting the lab. with dates, purpose(s) etc. would be maintained in register, which may be available for inspection, whenever required by the Competent Authority.

f) You would inform the RCGM through your Institutional Biosafety Committee (IBSC) the progress of work from time to time. The IBSC will collect all the information on experiments and would submit the consolidated information/data/ results on experiments to the RCGM once in a year.

g) Accidents or accidental release, if any, arising out of the experiments would be brought to the notice of the Govt. immediately.

h) You are required to confirm the acceptance of the above conditions to the DBT at your earliest convenience before starting the safety studies. You are further informed that you may contact the Department of Biotechnology for any clarification in the matter, which you may require.

PERIOD: The permit letter shall be in force from ____ to ____ unless it is sooner suspended or cancelled under the said Rules.

Kindly acknowledge the receipt of the same

(Member Secretary, RCGM)

Copy for information to :

1. The Chairman, GEAC, Ministry of Environment and Forests, Paryavaran Bhawan, CGO Complex, Lodhi Road, New Delhi-110 003
2. Office copy for file
3. Guard File

FORM D5

FORMAT FOR SUBMISSION OF SAFETY STUDIES OF rDNA PRODUCTS OF GENETICALLY MODIFIED ORGANISMS (GMOs)/ LIVING MODIFIED ORGANISMS (LMOs) FOR AGRICULTURAL AND ENVIRONMENTAL USE

1. **Name of the Applicant:** _____

   Designation: _____

   Address: _____

   Telephone No.: _____

   Fax No.: _____

   e-mail: _____

2. **DBT Office Memorandum No.:**
3. **Objectives of the proposal:**
4. **Summary of the products characteristics and process of development:**
5. **List of safety studies and protocols approved by RCGM**
   (please attach a copy of the approval letter):
6. **Safety study reports:**

   6.1 List of studies completed and deviations, if any from the approved protocols

   6.2 Dose calculation for conduct of safety studies

   6.3 Study reports (Each study report would reflect all the issues approved in the protocols). In addition the following to be included:

   - RCGM approval of protocol
   - IBSC approval of report
   - IAEC approval for animal use and for the procedures, if applicable
   - Quality assurance statement
   - Signatures of study director and all investigators who were involved in the study
   - All quality analytical reports on the test material and vehicle
   - Animal feed and animal health certifications

- Protocol deviations if any
- Discussion on the results
- Individual animal data, summary data and any other data like computer analysis outputs etc
- Conclusion

6.4 Address and accreditation status of the labs where these studies were conducted.

7. **Measures taken for containment:**

8. **Decontamination and disposal mechanisms:**

9. **Risk management (Emergency plan):**

10. **Any other relevant information:**

11. **Declaration:**

I declare that the information provided in the above format is correct and accurate to the best of my knowledge.

Date: **Signature of the Applicant**

Forwarded:

The proposal set out above has been considered and approved by the "Institutional Biosafety Committee" in its meeting held on _____ and is forwarded to RCGM for further necessary action.

Date: **Signature and name of the Chairman, IBSC**

Note:

1. Please submit 23 copies of the application along with the enclosures to the Member Secretary, RCGM, Department of Biotechnology for consideration by RCGM.
2. Enclosures should include
   - Copies of earlier approvals from RCGM
   - Copy of the minutes of IBSC meeting in which the proposal was approved
   - IBSC approval