भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
जैव प्रौद्योगिकी विभाग
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

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BT/BS/17/635/2015-PID

Date: 02nd September, 2020

OFFICE MEMORANDUM

Subject: Handbook For Institutional Biosafety Committee (IBSC), 2020

1. In accordance with "Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells 1989 (known as 'Rules, 1989') of the Environment (Protection) Act, 1986 (EPA 1986), an Institutional Biosafety Committee (IBSC) shall be constituted by an occupier or any person including research institutions handling microorganism/genetically engineered organisms. IBSC is to be constituted by every organisation engaged in research, use & applications activities related to GE organisms (organisms include microorganisms, animals, plants, arthropods, aquatic animals, etc.) and hazardous microorganisms (microorganisms include parasites, protozoa, algae, fungi, bacteria, virus, prions etc.) and products produced through exploration of such organisms. IBSC serves as the nodal point within an organization for implementation of the biosafety regulatory framework.

2. In the past few years, several reforms in Indian Biotechnology Regulatory Framework have taken place to ensure safe and secure use of biotechnological processes and products. The reforms include decentralized regulatory powers to IBSC and implementation of a user- friendly online mechanism of regulatory process through **Indian Biosafety Knowledge Portal (IBKP).**

3. In view of these changes, the Handbook for IBSC has been updated through extensive deliberations by the Expert Committee constituted for this purpose and the Review Committee on Genetic Manipulation (RCGM), DBT recommended the updated version.

   The updated handbook for IBSC provides information on regulatory processes to be followed for research activities while dealing with GE organisms & non-GE hazardous microorganisms in line with Rules, 1989 and guidelines issued by DBT from time to time.

4. It provides guidance for composition, constitution and functions of IBSCs including steps of application evaluation, approval procedure, monitoring, compliance and online submissions through IBKP portal.

5. The "Handbook For Institutional Biosafety Committee (IBSC), 2020" supersedes "Guidelines and Handbook for IBSCs" issued in 2011.

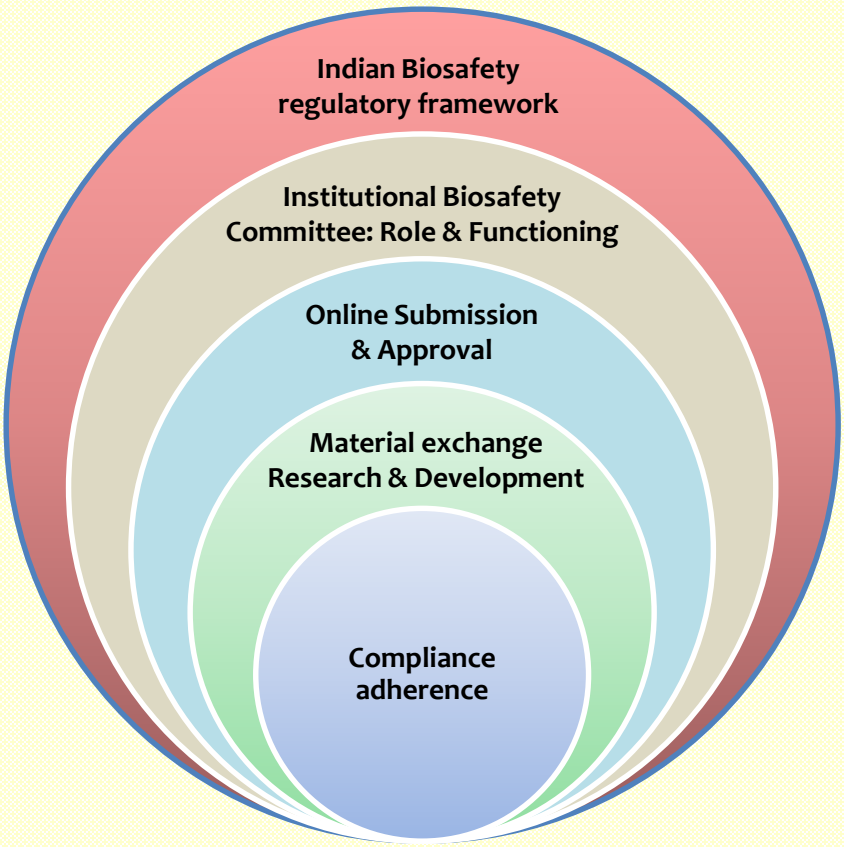
6. The "Handbook For Institutional Biosafety Committee (IBSC), 2020" is notified at www.dbtinida.nic.in & https://ibkp.dbtindia.gov.in/.

(Nitin Kumar Jain)
Member Secretary, RCGM
Scientist F, DBT

To,

1. All institutional Biosafety Committees
2. Communication Cell, DBT

HANDBOOK for INSTITUTIONAL BIOSAFETY COMMITTEES (IBSCs)



सत्यमेव जयते

Department of Biotechnology
Ministry of Science & Technology,
Government of India

Third Revised Edition September, 2020

सत्यमेव जयते

डॉ. रेणु स्वरूप
DR. RENU SWARUP

सचिव
भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
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GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
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Foreword

Department of Biotechnology has framed several guidelines/guidance documents from time to time to ensure safe use of r-DNA technology and hazardous microorganism in biotechnology research and development activities.

The guidance documents for various stakeholders particularly research scientists provides information on policies and practices to be followed in complying with rules and regulations for recombinant DNA technology based products and processes, as per the 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 and Climate Change (MoEF&CC), Government of India under the Environment(Protection) Act, 1986.

In 2004, DBT had released a "Handbook for IBSC Members", which was subsequently revised in 2011, and DBT released as the 2nd Revised Edition "Guidelines and Handbook for IBSC Members". The Handbook had proven to be instrumental in laying down the Principles and Practices for research and development across the country, including Institutes, Universities, Industries, Public and Private Platforms. Over these years, DBT has facilitated interaction with IBSCs and proactively introduced several reforms in Indian biotechnology regulation to facilitate use of new technologies their promotion, adoption, and popularization without compromising on safety and security concerns.

To facilitate the research regulatory ecosystem for biotechnology a total of 285 IBSCs are today functioning. The Department has also implemented online submission of applications to Review Committee on Genetic Manipulation through IBKP portal in year 2019. Further, the IBSCs have been empowered to take more responsibilities and appropriate decisions. Therefore, in order to strengthen the regulatory compliance, the need to harmonize the regulatory system at par with international standards and to consolidate the new developments, the handbook on IBSC has been revised. This third revised edition of the handbook provides updated information for compliance by IBSCs and procedures to be followed. The views of various stakeholders have been taken into consideration before finalizing the Handbook which has been duly adopted by RCGM.

I congratulate Dr. A.K. Rawat, Scientist 'G', DBT, Dr. Alka Sharma, Scientist 'G', DBT and Dr. Nitin Kumar Jain, Scientist 'F', DBT and Member Secretary, RCGM for working with the Chairman and all Members of RCGM and taking into consideration all issues required for strengthening the regulatory compliance by IBSCs. The contribution of the Biosafety Support Unit officials is also very valuable. I am confident that this third revised version of Handbook (2020) which includes general procedures, revised simplified procedures (2020), decentralized regulatory powers to IBSC and functioning of Indian Biosafety Knowledge Portal, would be beneficial for all the members of IBSCs. It would also accelerate DBT's efforts in creating awareness about updated regulatory procedures amongst scientists, researchers, biotechnology industries including start-ups policy makers as well as our budding scholars.

(Renu Swarup)

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सूचना का अधिकार

MINISTRY OF SCIENCE & TECHNOLOGY

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Prologue

As per the Indian biosafety regulations, organizations handling genetically modified organisms, recombinant DNA materials and non-GE hazardous microorganisms for research or production purpose should constitute an Institutional Biosafety Committee (IBSC) with the Department of Biotechnology approval. IBSC is one of the key statutory bodies, operating directly from the premises of the Institution and is responsible for proper implementation of Biosafety principles, rules, regulations and guidelines.

In the past, the Handbook editions mainly covered the composition, functions, role of IBSC, and application formats. In view of several reforms in Indian biotechnology regulation since then, there arises a need to update and revise the Handbook. In this third revised edition of the Handbook, decentralized regulatory powers to IBSCs and regulatory mechanism of online registration and renewal of IBSC at Indian Biosafety Knowledge Portal (IBKP; https://ibkp.dbtindia.gov.in), have been incorporated. Information on appropriate forms for submission of applications has been provided. Further, the competent authorities for approval of various applications have been described/ detailed.

We are pleased to acknowledge the critical inputs provided by Expert Committee constituted for this purpose, under the Chairmanship of Prof. P. Kondaiah (Indian Institute of Science, Bengaluru), esteemed members of the RCGM and various stakeholders during the revision process. We also acknowledge our sincere admiration and appreciation for the efforts by the RCGM Secretariat and Biosafety Support Unit, Regional Centre for Biotechnology throughout the preparation of the revised Handbook.

We are glad to present/release the "Handbook For Institutional Biosafety Committee (IBSC), 2020", for providing updated information on regulatory reforms and digital platform for all users.

Dr. A.K. Rawat
Adviser
Department of Biotechnology
Ministry of Science & Technology
Government of India

Dr.Nitin Kumar Jain
Member Secretary, RCGM &
Scientist-F
Department of Biotechnology
Ministry of Science & Technology
Government of India

About the Handbook

In compliance with “Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells 1989 (known as 'Rules, 1989') under the Environment (Protection) Act, 1986 (EPA 1986), an Institutional Biosafety Committee (IBSC) is to be constituted by every organisation engaged in research, use & applications activities related to GE organisms (organisms include microorganisms, animals, plants, arthropods, aquatic animals, etc.) and hazardous microorganisms (microorganisms include parasites, protozoa, algae, fungi, bacteria, virus, prions etc.) and products produced through exploration of such organisms.

IBSC serves as the nodal point within an organization for implementation of the biosafety regulatory framework.

In the past few years, several reforms in Indian biotechnology regulation have taken place to facilitate use of biotechnology, its promotion, adoption, and popularization without compromising safety and security concerns. The reforms include decentralized regulatory powers to IBSC and implementation of a user- friendly online transactions mechanism of regulatory process through Indian Biosafety Knowledge Portal (IBKP).

In view of these changes, the Handbook for IBSC has been updated. The handbook provides information on processes to be followed while dealing with GE organisms & non-GE hazardous microorganisms in line with Rules, 1989 and guidelines issued by DBT from time to time. The handbook describes the competent authorities under Rules 1989, constitution, composition, registration and renewal mechanism of IBSCs. It also provides roadmap of functions of IBSCs pertaining to steps of application evaluation, approval procedure, monitoring & compliance, and online transactions through IBKP.

The handbook supersedes “Guidelines and Handbook for IBSCs” issued in 2011.

Contents

ABBREVIATIONS

ABSL	-	Animal Biosafety Level
AqBSL	-	Aquatic Organism Biosafety Level
BC	-	Biological Containment
BSL	-	Biosafety Level
BRL	-	Biosafety Research Level
DBT	-	Department of Biotechnology
DLC	-	District Level Committee
EPA	-	Environment (Protection) Act, 1986
GE	-	Genetically Engineered
GEAC	-	Genetic Engineering Appraisal Committee
GLSP	-	Good Large Scale Practices
GOI	-	Government of India
GMO	-	Genetically Modified Organisms
HMO	-	Hazardous Microorganism
IBSC	-	Institutional Biosafety Committee
IBKP	-	Indian Biosafety Knowledge Portal
IBSL	-	Insect/Arthropod Biosafety Level
LMO	-	Living Modified Organisms
MoEF&CC	-	Ministry of Environment, Forest and Climate Change
NBPGR	-	National Bureau of Plant Genetic Resources
PBSL	-	Plant Biosafety Level
PI	-	Principal Investigator (R&D/Industry/Others)
PPE	-	Personal Protective Equipment
RCGM	-	Review Committee on Genetic Manipulation
RDAC	-	Recombinant DNA Advisory Committee
rDNA	-	recombinant DNA
RG	-	Risk Group
SBCC	-	State Biotechnology Co-ordination Committee

CHAPTER-I: INDIAN BIOSAFETY REGULATORY FRAMEWORK

1.1 BIOSAFETY REGULATORY FRAMEWORK

In India, all activities related to Genetically engineered organisms (GE organisms) or cells and non-GE hazardous microorganisms 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 (known as 'Rules, 1989') notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India, under the Environment (Protection) Act, 1986 (EPA 1986).

The mandate and function of Competent Authorities entrusted with implementation of biosafety regulations under Rules 1989 are:

Competent Authorities	**Mandate & Functions**
Recombinant DNA Advisory Committee (RDAC)	The RDAC functions in Department of Biotechnology (DBT) and shall review developments in biotechnology at national and international levels and shall recommend suitable and appropriate safety regulations for India in recombinant research, use and applications from time to time
Institutional Biosafety Committee (IBSC)	The IBSC is constituted by an occupier or any person including research institutions, handling hazardous microorganisms/ genetic engineered organisms {at Research & Development (R&D) level}. The occupier or any person including research institutions shall prepare, with the assistance of the IBSC, an up-to-date on site emergency plan according to the manuals /guidelines of the RCGM and make available copies to the DLC/SBCC and RCGM/GEAC.
Review Committee on Genetic Manipulation (RCGM)	RCGM functions in the DBT to monitor the safety related aspects in respect of on-going research projects and activities involving genetically engineered organisms/hazardous microorganisms. It shall bring out Manuals of guidelines specifying procedure for regulatory process with respect to activities involving genetically engineered

	organisms in research use and applications including industry with a view to ensure environmental safety. All ongoing projects involving high risk category and controlled field experiments shall be reviewed to ensure that adequate precautions and containment conditions are followed as per the guidelines. RCGM shall lay down procedures restricting or prohibiting production, sale, importation and use of such genetically engineered organisms of cells as are mentioned in the Schedule of Rules, 1989.
Genetic Engineering Appraisal Committee (GEAC)	The GEAC functions in the MOEF &CC and is responsible for approval of (i) activities involving large scale use of hazardous microorganisms and recombinants in research and industrial production from environmental angle (ii) proposals relating to release of genetically engineered organisms and products into the environment including experimental field trials. The committee or any person/s authorised by it shall have powers to take punitive actions under the Environment (Protection) Act, 1986.
State Biotechnology Coordination Committee (SBCC)	SBCC reviews periodically the safety and control measures in the various installations/institutions handling genetically engineered organisms/hazardous microorganisms. SBCC have powers to inspect, investigate and take punitive action in case of violations of statutory provisions through the Nodal Department and the State Pollution Control Board/Directorate of Health &/ Medical Services
District Level Committee (DLC)	DLC monitors the safety regulations in installations/institutions engaged in the use of genetically modified organisms/ hazardous microorganisms and its applications in the environment. DLC/or any other person/s authorized in this behalf shall visit the installation engaged in activity involving genetically engineered organisms, hazardous microorganisms, formulate information chart, find out hazards and risks associated with each of these installations and coordinate activities with a view to meet any emergency. DLC shall also prepare an off-site emergency plan for field trials. The District Level Committee shall regularly submit its report to the State Biotechnology Coordination Committee/Genetic Engineering Approval

	Committee.

While the RDAC is advisory in functions, IBSC, RCGM and GEAC are involved in regulatory and approval functions. SBCC and DLC are responsible for monitoring the activities related to GMOs at state and district levels respectively.

1.2 SCOPE OF THE HANDBOOK

This handbook covers roles and responsibilities of IBSC relevant to Rules 1989. This handbook shall guide online registration and functioning of IBSC, submission of forms and other activities.

CHAPTER-II: INSTITUTIONAL BIOSAFETY COMMITTEE

In compliance with Rules 1989, an Institutional Biosafety Committee (IBSC) is to be constituted by every organisation engaged in research, use & application activities related to GE organisms (organisms include microorganisms, animals, plants, arthropods, aquatic animals, etc.) and hazardous microorganisms ("microorganisms" shall include all the bacteria, viruses, fungi, mycoplasma, cells lines, algae, protodones and nematotes). IBSC is the nodal agency within an organization for implementation of the biosafety regulatory framework. DBT/RCGM has been entrusted with registration and monitoring of IBSCs.

Institutional Biosafety Committee (IBSC) is solely responsible:

i. To implement and respond to institutional biosafety & biosecurity at the institution level and

ii. Evaluation of applications/ reports related to rDNA technology work involving the GE organisms and non-GE hazardous microorganisms in an organisation.

2.1 RESPONSIBILITIES AND FUNCTIONS OF IBSCs

a) Assess and monitor the items of general consideration i.e. research facilities, procedures and experts involved in HMOs/GMOs/LMOs and GE research and ensure that the proposed risk assessment, risk management and emergency plans are sufficient.

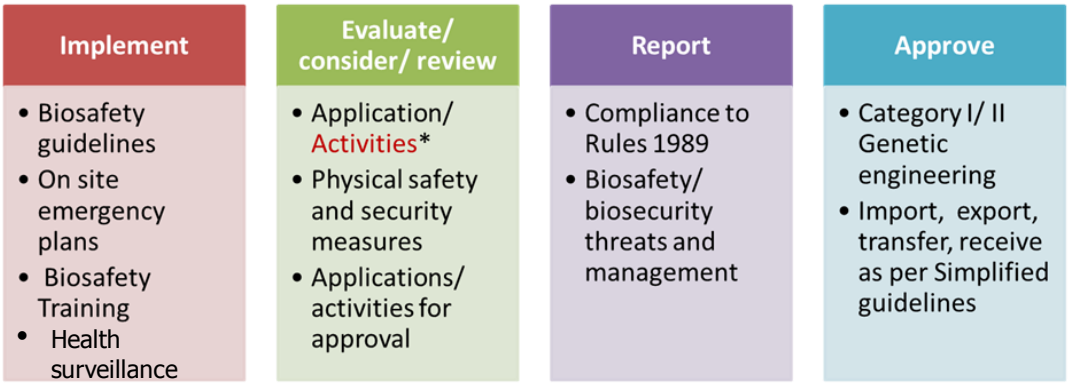
b) Provide guidance to Principal Investigator on the issues related to biosafety while using HMOs/GMOs/LMOs and GE research including safety of the researcher(s) associated with the work.

c) Inform the Principal Investigator about IBSC review, approval or rejection of applications.

d) 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, 1989e). The IBSC shall inspect laboratories using checklists. IBSC shall apprise short coming measures (if necessary) under information to Head of Organisation. Inspection reports should be maintained in the IBSC.

e) Reporting for incidents and release: It is necessary that any incident within an organisation such as non-compliance of the biosafety guidelines, any biosecurity issues or any significant research-related accidents and illnesses be reported to IBSC/ RCGM.

The primary function of the IBSC is to implement and ensure compliance of provisions of Rules 1989 at the Institutional level. These functions include:



* Activities include import, export, transfer, receive, contained (laboratory) and confined R&D involving GE organisms and/or hazardous microorganisms.

2.2 REGISTRATION OF IBSC AT IBKP

Constitution of an IBSC and its registration in DBT through Indian Biosafety Knowledge Portal (IBKP) is mandatory in India for every organization working with GE organisms, cells and hazardous microorganisms under Rules 1989. Without registration/renewal of the IBSC, the institution/organization shall not be eligible to conduct any rDNA activities and research on hazardous microorganisms that fall under the purview of Rules 1989. Any modification/ update of information of a registered IBSC and renewal of IBSC shall also be made through IBKP. Only the utmost authority of the organization or his/her designate (suitably a senior competent officer) who shall serve as the Chairperson, IBSC; shall register the institution/organization online at IBKP.

The following two steps need to be completed for the registration of an IBSC at IBKP portal:

i) **Step 1 - *Organisation registration:*** The organisation seeking to constitute IBSC has to first register their organisation online at IBKP (https://ibkp.dbtindia.gov.in/content/ibscinfo). After verification of the details, permanent login ID will be provided for each Organization through an email. This step is a mandatory for registration of IBSC.

ii) **Step 2 - *IBSC registration*:** Using the Organization's permanent login ID and a password generated by the competent authority of the organization or his/her designate, the organisation shall submit form for registration of IBSC on the IBKP portal. with brief bio-data and consent letters of the proposed IBSC members including DBT nominee; proposed activities involving hazardous microorganisms, GE organisms and products thereof to be carried and availability of containment facilities to carry out the desired research.

After verification of details in the registration form, the request would be considered and appropriate decision taken be communicated to the organization through the portal. In case of any deficiencies/ clarifications, the same would be communicated to the organisation through the portal.

INDIAN BIOSAFETY KNOWLEDGE PORTAL (IBKP)

As part of Digital India initiative of Government of India, Department of Biotechnology (DBT) has launched a web portal namely **India Biosafety Knowledge Portal (IBKP)** to make regulatory transactions online and paperless. The IBKP may be accessed through DBT website (http://dbtindia.gov.in/ or https://ibkp.dbtindia.gov.in)

The IBKP is a platform for all the stakeholders i.e. applicant, IBSC, RCGM members, where it provides information on:

- ✓ Relevant Acts and Rules related to Biosafety of GMOs/LMOs in India.
- ✓ Guidelines on Biosafety, Biocontainment, Checklists.
- ✓ Database on various ongoing research activities on GMOs/LMOs and products thereof in the country including scientific Risk Assessment and Risk Management Plans (RARMPs).
- ✓ Linkages to international developments and scientific information.
- ✓ IBSC registrations/renewals and annual compliance records.
- ✓ Online submission of Forms for Import/Export/Research & development projects, Pre-clinical toxicity of recombinant DNA derived Biosimilars and Investigational New Drug (IND), Event selection trials, Biosafety Research Level 1 trial, etc. including online tracking of the application status.
- ✓ Modules showcasing steps of online transactions.

Homepage of India Biosafety Knowledge Portal (IBKP) (https://ibkp.dbtindia.gov.in)

2.3. CONSTITUTION OF IBSC

The IBSC shall comprise of a Chairperson, Member Secretary, Biosafety Officer, a DBT nominee and at least four scientists engaged in rDNA work (at least one each from within and outside the organization) as members.

Composition	Criteria
Chairperson	The Head of the organisation or his/her designate (suitable senior officer) shall be the Chairperson (utmost authority) of the IBSC. The Chairperson should preferably have knowledge and experience in scientific research pertaining to GE organisms, latest technological developments in the area & handling of hazardous microorganisms.
Member Secretary	One of the internal members should be designated as Member Secretary.
Biosafety Officer	Each IBSC shall have a member with medical qualifications designated as Biosafety Officer. The Biosafety Officer should be adequately trained with good lab practice in handling RG3 & RG4 pathogenic agents that require special containment conditions (Biosafety Level 3 or 4 facilities) and be able to offer advice on specialized containment requirements.
DBT Nominee	Each IBSC shall have an outside expert nominated by DBT who oversees the activities to ensure that biosafety aspects are being fully adhered by the organisation. While seeking registration of IBSC, the organization shall suggest 3 outside experts working in the areas preferably from nearby institutions. DBT may nominate one among them as DBT nominee or may nominate any other suitable expert as DBT nominee.
Internal and External members	IBSC shall have at least four members with at least one internal and one external member, preferably scientists engaged in rDNA work & non-GE hazardous microorganisms.

IBSC may associate/ invite qualified experts/ consultants from within or outside organisation as and when required to seek advice on specific scientific/ technical matters. Participation of such external experts/consultants in meeting should be recorded in the minutes. Opinion of

the expert along with rational of the recommendation should be submitted along with the application.

2.4 ROLES/ RESPONSIBILITIES OF IBSC MEMBERS

2.4.1 Chairperson, IBSC

- Has awareness of all requirements regarding compliance with the Rules, 1989 and other regulations related to HMOs/GMOs/LMOs/ and products derived thereof and ensure that the biosafety guidelines are followed in their organisation.
- Ensures that the available facilities at the organisation are adequate to meet the biocontainment levels stipulated while working with Hazardous microorganisms and GE organisms as per the latest guidelines while approving or forwarding applications.
- Ensures that training of IBSC members and Laboratory Personnel are being conducted on regular basis.
- Ensures that regular meetings of IBSC are held to review research projects in the organisation; open discussion takes place amongst the members in the meetings and the views of external members as well DBT nominee are recorded in the minutes. All decisions and approval need to have concurrence of DBT nominee.
- Ensures on-site biosafety & emergency plan are in place and decontamination & disposal mechanisms for laboratory and biomedical waste are in place as per the latest DBT Guidelines and also in accordance the guidelines issued by Central Pollution Control Board (CPCB) and local authorities.
- Ensures that in case of any accidental release, the concerned Scientist/Principle Investigator must immediately bring it to the notice of the Chairperson, IBSC who would be responsible for ensuring containment of the released organism(s) and informing the regulatory bodies (RCGM/GEAC) in the stipulated timeframe.

2.4.2 Member Secretary, IBSC

- Acts as a focal point for compliance with rDNA safety guidelines, good lab practices, biological containment etc.
- Be responsible for reporting and communication with RCGM with respect to functioning of IBSC in an organization.

- Ensures to organise regular meetings of IBSC and maintain updated documents such as agenda, minutes of meetings and other related papers for proper record keeping.
- Ensures that IBSC minutes and applications considered in the meeting are submitted through **IBKP portal within 7 days of meeting**.
- Ensures that annual reports in the prescribed proforma and medical surveillance reports are submitted at IBKP portal **on or before 15th February of each year**.
- Provides technical advice to Principal Investigator about safety procedure and containment facility as per the guidelines issued by DBT.

2.4.3 Biosafety Officer

- Ensures that biosafety measures are in place to prevent the accidental escape of hazardous microorganisms and GE organisms.
- Wherever there is a BSL3/4 facility, Biosafety officer must be trained to familiarise with BSL-3 and 4 facilities and be responsible for monitoring such facilities and health of workers in the facility.
- Undertake periodic laboratory inspections specially BSL-3 and BSL-4 facility.
- Assist Project Investigators (PI) in developing emergency plans for containment and clean-up of investigates, accidental releases, if any etc. and review emergency plans from time to time to prevent any lab accidents.
- Prepares Medical Surveillance Reports for people working in BSL 3 or 4 facilities in the performa available on IBKP of all laboratory personnel annually and submit to Member Secretary for uploading online at IBKP before commencement of rDNA work by PIs.
- Review and report to the Head of the organisation and Member Secretary, IBSC, DBT nominee of any non-compliance of guidelines / health issues of staff.

2.4.4 DBT Nominee, IBSC

- Serves as the link between DBT-RCGM and the respective IBSC

- Ensures that the IBSC reviews all ongoing activities.
- DBT nominee must ensure compliance of all relevant guidelines.
- Ensures that all the activities carried out in the organization are within the purview of the DBT guidelines and guide the IBSC on all biosafety matters including compliances.
- Iincludes an assessment report of on-site inspection of the available facilities in the IBSC meetings.
- If any new pathogen/ higher Risk group organism (RG 3&4) is to be used by the organization, the DBT nominee shall assess the capacity and infrastructure to conduct the experiments in the organisation and include that in the IBSC meeting minutes.
- In case of any accidental release, the IBSC Chairperson must inform DBT nominee at the earliest. The DBT nominee must then review the safety measures taken and accordingly, send an independent report on the “accidental release” highlighting any non-compliance of guidelines / health issues of staff to the Member Secretary, RCGM within 48 hrs.

2.4.5 Internal and External Members

- Review all submitted applications as per the guidelines and checklist (refer to Section functions of IBSC).
- Participate in the training programs organized by IBSC to train researchers on biosafety and Biosecurity aspects.

2.5 CONFIDENTIALITY AGREEMENT

All IBSC members are expected to maintain confidentiality 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. Each IBSC member including Chairperson, Biosafety Officer, DBT nominee, Member Secretary and internal/external experts shall sign confidentiality agreement in the performa available on IBKP at the time of constituting IBSC or effecting changes in the composition of IBSC.

2.6 TENURE AND RENEWAL OF IBSC

- The tenure of the IBSC is for a period of 3 years from the date of issue of approval letter. The institute has to renew IBSC registration after every three years. IBSC shall process renewal request through portal at least 3 months before the expiry date of the current validity period.
- Registered IBSCs requesting for major changes in the IBSC composition including the change of DBT nominee may request for renewal of IBSC during the validity period.
- Renewal of the IBSC shall be made through the 'Renew IBSC Registration' module of the IBKP.
- After verification of details in the registration renewal form, RCGM shall approve the registration and communicate the same through the portal to the organisation. In case of any deficiencies/ clarifications, the same would be communicated to the organisation through the portal.

2.7 CHANGES DURING THE TENURE OF IBSC

Registered IBSCs can request for update of information provided at the time of registration through the portal. Updation of changes in IBSC details including minor changes in the IBSC composition should be submitted with reasons/ justifications and proposed changes at IBKP portal at least two weeks before the date of proposed change.

The steps involved in the IBSC modification request process are:

i) Using the Organization's permanent login ID and password, Chairman/ Member Secretary, IBSC need to access the IBSC dashboard.

ii) Relevant changes may be made in the "Modify IBSC registration" section where any change shall appear in red colour.

iii) After submitting application for modification online, the content would be verified.

iv) After verification of details in the registration form, the request would be considered and appropriate decision taken would be communicated to the organisation through the portal. In case of any deficiencies/clarifications, the same would also be communicated to the organisation through the portal.

2.8 IBSC MEETINGS AND RECORDS

2.8.1 Regular IBSC Meetings

The IBSC shall review and approve/ recommend the applications. There is no restriction on number of meetings to be held by IBSC. However, a minimum of two meetings must be held in a year within the institutional premises, in compliance of biosafety regulations. In case, organizations are involved in working with Risk Group 3 and above organisms or Category III and above experiments, IBSC must meet every quarter to ensure safety compliance.

2.8.2 Quorum for conducting IBSC meeting

At least 50% of the IBSC members must be present to conduct the meeting. No meeting shall be held in the absence of Chairperson, Member Secretary, Biosafety Officer and DBT nominee. The final approval or disapproval of non-exempt projects of HMOs/GMOs/LMOs/rDNA requires a majority vote by IBSC members and consent of DBT nominee.

2.8.3 Emergency IBSC Meetings

The Chairperson, IBSC may call an emergency meeting, to address any urgent issue such as non-compliance or unexpected events involving GE organisms, hazardous microorganism and rDNA materials in an organization.

2.8.4 Minutes of IBSC meetings

The minutes of the IBSC meetings are to be filled online at the portal. The approved minutes signed by all members present must be uploaded at the portal for approval by RCGM.

IBSC minutes should be self-contained and should cover:

i) Review of organisation, availability of contained facilities and trained manpower as mentioned under General Consideration;

ii) Scientific Considerations based on which IBSC approved the proposal or recommended to RCGM for approval;

iii) HMOs/ GMOs/ traits with quantities approved/ recommended to RCGM;

iv) It is mandatory to provide the duly signed attendance sheet.

In case of applicant initiating work involving RG3 and above organism or Category III experiment, DBT nominee shall visit the site and provide comments on adequacy of facility to conduct such work while recommending the application by IBSC. All decisions and approval during IBSC meetings must have concurrence of DBT nominee. In case of any dissent, the opinion of DBT nominee needs to be recorded in IBSC minutes.

2.8.5 Conflict of Interest

IBSC members who have a conflict of interest in a project should not be present during the deliberations of that project in the meeting and the same must be recorded in the IBSC minutes.

2.8.6 IBSC Records

Each IBSC has to maintain the following records (in hard and soft copies):

- Approved and duly signed minutes of IBSC meetings including attendance sheets.
- Annual report of all ongoing GE organisms/hazardous microorganisms projects.
- Copies of applications considered and approved by IBSC.
- Applications forwarded to RCGM or GEAC.
- Other documents such as statements regarding conflict of interest, confidentiality agreements signed by members.

2.8.7 Training

IBSCs must provide training on the issues related to biosafety to all the researchers while using HMOs/GMOs/LMOs/rDNA materials. At the R&D stage, 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. It is therefore extremely important that the research and laboratory staff is well trained in biosafety measures.

2.8.7.1 Training of IBSC Members

It is the responsibility of the Head of the Organisation to arrange training for the members of IBSC including Chairman IBSC on biosafety frameworks, the Rules, 1989, related regulations and guidelines. Biosafety officer shall be adequately trained to monitor BSL-3 or BSL-4 laboratory whenever such facilities are in operation in the organization.

2.8.7.2 Training of Laboratory Personnel

General biosafety training is mandatory for all individuals conducting research with GMOs/LMOs/GE materials and Hazardous Microorganisms. Such training may be organized by the organization itself or through experts. This includes knowledge in handling of organisms, approved decontamination approaches 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 facilities must go through BSL-3 or BSL-4 laboratory specific training before using the facility. Records/ information pertaining individuals trained on such facilities in the institute to be maintained by the IBSC.

CHAPTER-III: ONLINE SUBMISSION OF FORMS AND APPROVAL PROCESS

IBSCs are responsible for assessing and monitoring the research involving in GMOs/LMOs/GE and hazardous organisms and ensure that the proposed risk assessment, risk management and emergency plans are sufficient. To achieve this objective, IBSCs need to ensure proper training is provided to all the IBSC members and researchers of the organisation. IBSCs at the institutional level are responsible for the assessing the research being conducted and providing approval to the submissions and recommending all the research applications to the RCGM for its consideration. The above mentioned points would be discussed in detail in this chapter.

3.1 SUBMISSION OF APPLICATION FORMS AT THE IBKP PORTAL

For conducting research in the organisation, the Principal Investigators (PIs) must apply online by filling appropriate application form before initiating research. The application forms are available at the IBKP portal. The online application forms are to be filled and submitted for consideration by institute's IBSC and then by RCGM. The forms would be accessible to all the registered IBSCs on the portal. IBKP hosts application forms for import, export, transfer and R&D at contained (laboratory) and confined (field trial) activities specific for healthcare, agriculture and environmental use. All forms are interactive in nature where applicant can submit the application required information along with required enclosures in relevant application proforma. The List of Forms/Performa available on IBKP are available at Annexure-I.

3.1.1. Providing Sub-User access through the IBKP portal

In view of multiple investigators from an organization being involved in work related to genetic engineering and/or hazardous microorganism that requires approval of IBSC and/or RCGM, the portal has a provision where the Chairperson, IBSC can issue sub-user access to investigators to enable them to access the application forms. The salient features of sub-user access to portal are:

i) The Chairman/ Member Secretary of the IBSCs having the login ID of the IBSC may provide access of the portal to the PIs for accessing and filling the application forms.

ii) Information submitted by a Sub-user (PI) will not be visible to other sub-users. However, all applications submitted by sub-user shall be visible to the authority holding the permanent IBSC log in ID and password.

iii) No other functions like change of IBSC information, compliance submission, etc. would be possible through sub-user access.

The applicant needs to select the appropriate area and subsequently select appropriate form specific to the intended purpose from the drop-down menu provided at the "RCGM Dashboard" of the portal.

3.1.2. Process for online submission of applications at IBKP

- Using sub-user access credentials, applicant needs to access RCGM dashboard and initiate the online application filling process through 'submit new application' tab.
- From time to time, the forms will be auto-saved preventing loss of information filled in the process or else the applicant may save the document periodically.
- Periodically, Member Secretary, IBSC shall prepare agenda by including all the applications filled by sub-users and circulate agenda along with all applications one week in advance to be considered for convening the meeting of IBSC.
- Once IBSC minutes are approved, Member Secretary will fill the IBSC approval details & upload IBSC minutes (preferably within a week of holding the meeting but no later than 15 days) and submit the application for consideration by RCGM.
- Only a completely filled application form will be accepted for consideration. The applicant shall ensure correctness of the information provided in the form. Once submitted, the information cannot be changed.
- On successful submission, the applicant shall receive intimation through registered email id and the same will be reflected in the notification panel of the portal.
- Each application will get a Unique Authorization Code (UAC code) which may be used by the applicant to track the status of application at IBKP.

- After verification of details in the submitted Application form, the application may be considered and decision taken be communicated to IBSC so as to provide RCGM recommendation to PI. In case of any deficiencies/ clarifications, the same would be communicated to the IBSC through the portal to intimate PI for necessary actions. The information would be noted down in subsequent RCGM meeting.

3.2 COMPETENT AUTHORITIES FOR APPROVAL OF APPLICATION FORMS

IBSC shall review and process the applications for approval of the competent authorities as per Rules, 1989. IBSC must ensure that approval of competent authorities (i.e. IBSC, RCGM & GEAC) has been obtained before commencement of rDNA work on a case-to-case basis.

The pathways for processing applications/ reports for approval of competent authorities for bio-pharma and agriculture sectors are provided at **Annexure-II**.

In brief, the approval of various category of experiments by competent authorities are given below:

3.2.1 Processing the applications for approval of IBSCs

IBSC shall review and evaluate capabilities of the organization to undertake the proposed rDNA research activities specially those involving high risk group (RG3 and RG4) organisms and Category III and above experiments. The 'Regulations and Guidelines on Biosafety of Recombinant DNA Research & Biocontainment, 2017' have classified GE experiments into three categories (Category I, II & III) with increasing risk concerns and respective competent approval authorities. Depending on the organism involved in GE experiments to be performed, the categories of GE experiments and biosafety level facilities are summarized below in Table 1 & 2 respectively.

- Category I GE experiments, the sub-user should intimate the IBSC about the objective and experimental design of the study along with organisms involved.
- Category II GE experiments require prior authorization from IBSC before the commencement of the experiments through submission of information in the prescribed proforma.
- IBSC may permit the Import/ Export/ Transfer/ Receive of regulated items of specified quantities for Biopharma R&D purpose of Drug Development and R&D purpose under "Revised Simplified Procedure/Guidelines on Import, Export and Exchange of Regulated items, 2020" (Annexure-III).

- In case of export of biological materials belonging to Special Chemicals, Organism, Materials, Equipment & Technologies (SCOMET) category, the applicant needs to apply to Directorate General of Foreign Trade (DGFT), Ministry of Commerce after approval from IBSC/ RCGM ion from IBSC (www.dgft.gov.in). In case of GM plants and planting materials, the import is routed through the Director, National Bureau of Plant Genetic Resources (NBPGR) of the Indian Council of Agricultural Research, on the basis of the authorization letter issued by the RCGM Secretariat.

- As per the 134th GEAC recommendations, IBSCs are permitted to conduct event selection trials within the organization/company owned premises without the requirement of NOC from State Governments. In all such cases, IBSC must follow "Guidelines for the conduct of confined field trials of regulated, GE plants (http://www.geacindia.gov.in/resource-documents/biosafety-regulations/guidelines-and-protocols/Guidelines_for_Confined_Filed_Trials_of_Regulated_Genetically_Engineered_GE_Plants.pdf) and adhere to Standard Operating Procedures (SOPs) for confined field trials of regulated, GE plants, 2008 (http://www.geacindia.gov.in/resource-documents/biosafety-regulations/guidelines-and-protocols/Standard-Operating-Procedures-for-confined-field-trials.pdf)

TABLE 1. Categorization of GE Experiments and Approval requirements

S. No.	GE experiments on					Approvals
	Microorganism	Animals	Plants	Insects	Aquatic animals	
Category I	Insertions of gene into RG 1 microorganism having no adverse health, phenotypic or genotypic consequence. Experiments involving approved host/vector systems provided that the donor DNA is originated from RG 1 microorganism. Self-cloning, fusion of protoplasts between non-pathogenic RG 1 organism, etc.	Breeding, housing and experiments of gene 'knockout'. Breeding of GE animals transformed with sequences of viral vector belonging to RG 1. Research involving the introduction of nucleic acids into animals provided that the nucleic acid does not give rise to any infectious agent.	Research & development, and maintenance of GE plants harbouring DNA from Risk Group 1 microorganism. Working with plants for the development/improvement of transformation protocols. Genome editing leading to SDN1-type mutations.	GE arthropods with genes from RG 1 microorganisms and other non-pathogenic organisms provided the genetic engineering process has no, or only negative effects on viability, survivorship, host range, or vector capacity. Challenged or infected with GE microorganisms that fall under RG 1.	GE aquatic animals containing genes from RG 1 microorganisms. Challenged or infected with GE microorganisms that fall under RG 1.	An investigator should intimate the IBSC of the study objectives and experimental design along with organisms involved. IBSC should review the same as and when convened for record purpose, monitoring or action to be taken, if any.

Category II	Work with non-approved host/vector systems where the host or vector does not cause disease in plants, humans or animals. Experiments with approved host/vector systems, in which the gene inserted is a pathogenic determinant. Experiments on RG2 microorganisms in the presence of helper virus Experiments in which DNA from RG 2 or 3 organism is transferred into non-pathogenic prokaryotes or lower eukaryotes host vector system.	Experiments with GE animal and associated materials, harbouring DNA from a RG 2 microorganism. Experiments with animals infected with GE microorganism (s) that fall under Risk Group 2.	Research & development, and maintenance of GE plants harbouring DNA from Risk Group 2 microorganism. Experiments on GE plants conferring herbicide tolerance or pathogen resistance. Genome editing leading to SDN 2 and 3 -type modifications.	GE arthropods with genes from RG 2 microorganisms and other non-pathogenic organisms provided the genetic engineering process has no, or only negative effects on viability, survivorship, host range, or vector capacity. Challenged or infected with GE microorganisms that fall under RG 2.	GE aquatic animals containing genes from RG 2 microorganisms and other non-pathogenic organisms provided the genetic engineering process does not increase virulence and environmental fitness of the organism. Challenged or infected with GE microorganisms that fall under RG 2	An investigator requires prior authorization from IBSC before the commencement of the experiments.
Category III and above	Experiments on RG 2 and RG 3 microorganisms where insertion of gene directly involved in production of toxin or allergen or antimicrobial compounds.	Experiments with animals infected with GE microorganisms that fall under RG 3. Experiments on animals using DNA which encodes a vertebrate toxin.	Growing genetically modified plants containing genes from microorganisms that fall under RG 3. Experiments involving GE plants containing genes directly involved in the production of toxins/allergens	GE arthropods with genes from RG 3 microorganisms and other pathogenic organisms. Challenged or infected with GE microorganisms that fall under RG 3.	GE aquatic animals containing genes from RG 2 microorganisms where the genetic engineering positively affects environmental fitness and virulence Challenged, infected with RG 3 microorganisms.	An investigator requires prior authorization from IBSC and subsequent approval from RCGM before the commencement of experiments.

Table 2. Category of experiments, GE organism involved and Biosafety Level Facility Requirements

Category	GE Microorganisms	GE Animals	GE plants	GE Insects	GE Aquatic organisms
Category I	BSL-1	ABSL-1	PBSL-1	IBSL-1	AqBSL-1
Category II	BSL-2	ABSL-2	PBSL-2	IBSL-2	AqBSL-2
Category III and above	BSL-3/BSL4	ABSL-3	PBSL-3	IBSL-3	AqBSL-3

3.2.2 Processing the applications for information/ approval of RCGM

IBSC shall review and authorize PI (sub-users) to submit applications to RCGM for Import, Export, Transfer, and Receive of regulated items

- Those items not covered in the "**Revised Simplified Procedure/Guidelines on Import, Export and Exchange of Regulated items for R & D purpose, 2020**" will require approval from RCGM.
- All materials belonging to RG3 and RG4 require prior approval of IBSC followed by RCGM for Import, Export, Transfer, Receive and R&D activities.
- Category III Activities involving Research, Production, Preclinical Studies of HMOs/GMOs in Healthcare and Other Studies
- To inform RCGM to carry out Research and Development involving HMOs/ GMOs/LMOs for Healthcare and Industrial use.
- To submit application to RCGM to conduct Preclinical and/or Safety Studies of Similar Biologic developed using HMOs/GMOs/LMOs for Healthcare and Industrial Use.
- To submit application to RCGM to conduct preclinical and/or Safety Studies of New DNA Products developed using HMOs/GMOs/ LMOs.
- To submit report to RCGM of preclinical or other safety studies of Similar Biologic/ New rDNA Product developed using HMOs/GMOs/LMOs. IBSC shall co-opt subject experts to review PCT reports and submit to RCGM along with the comment of subject expert.
- Activities involving Research, and Safety studies of GE Plants.
- To inform RCGM to carry out R&D involving HMOs/GMOs/ LMOs for Agricultural and Environmental Application.
- To submit application of Event Selection, BRL-1 and other studies to RCGM to undertake CFT and to undertake safety studies of GE Crops/ Plants for Agricultural and Environmental use.
- To submit report to RCGM of Safety Studies of GE Crops/Plants for Agricultural and Environmental Use.

- To submit Report to RCGM of Safety Studies of HMOs/GMOs/ LMOs other than GE Crops/ Plants for Agricultural and Environmental use
- To submit Report to RCGM on Restricted Release Research Study(s)/ Trial(s) of GE Arthropods for Agricultural, Healthcare and Environmental use

3.2.3 Other approvals required

Apart from the approval of IBSC and RCGM, the GE activities may require approvals from other regulatory agencies.

Approval from GEAC, CDSCO, NBA, DHAD, DGFT, Plant Quarantine Authorities, Animal Ethics Committee, NOC from State Government in case of field trials etc. as required is applicable.

3.3 EVALUATION OF APPLICATIONS BY IBSCs

Safety assessment of each application based on scientific knowledge and experience must be done by IBSCs. Some logical steps that need to be followed for review of a project proposal in the context of safety assessment by IBSC are given below. It may be noted that this list is indicative and specific additions/deletions or modifications shall be made to suit the requirements of each project on a case-to-case basis.

3.3.1. Molecular Biology

i. Characteristics of the donor/source organisms

If the insert contain genes which are biologically active, producing toxins or virulence/pathogenic factors, then characteristics of the donor/source organism is extremely important for risk consequence. If the donor organism is merely used as a source of well-characterized gene or DNA sequence coding a specific trait or a promoter or other regulatory sequence, the characteristics of the source organism may or may not be critical consideration for additional safety considerations.

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

ii. Characteristics of the host/recipient organisms

The characterization of the host/recipient organism provides the starting point for the risk assessment. 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. The documented evidence on the safe use of the host organism, if available, should be considered. The general assumption is that the level of risk associated with the genetically modified organism is at least as great as that of the host organism (wild type), until proven otherwise.

iii. Characteristics of the modification/ insert/ gene construct

The properties of the insert/gene construct are extremely important in risk assessment of GMOs. Individual components used in the preparation of the construct i.e. regulatory sequences (promoters, enhancers, etc.), selectable markers and other genes that do not get transformed themselves but aid the process to achieve desired base pair changes and insertion of foreign DNA (eg. CRISPER/Cas9) require careful review and safety assessment.

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 in 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 presence of genes coding for antibiotic resistance might be of serious concern, although some of the antibiotic resistance genes used in the vectors are commonly found in the environment.

The method of transformation used for introducing the required gene(s) should be considered for the risk assessment of the modified organism as copy number of transgenes and site of integration vary significantly depending on the method followed. For example, in case of plants, the two principle methods of transformation that are widely used are the *Agrobacterium* mediated transformation and particle bombardment. While *Agrobacterium* mediated transformations result in a low transgene copy number, minimal rearrangement and higher transformation efficiency; particle bombardment causes extensive rearrangements to transformed sequences. Similarly, emerging technologies such as genome editing should be considered for the risk assessment of the modified organism from non-targeted modifications in the genome point of view.

v. Characteristics of the modified organism

Molecular characterization provides information about the composition and integrity of inserted DNA, the number of copies of inserted DNA, the number of sites of insertion, evidence confirming desired modification/editing and non-target modifications, if any, and the expression level of introduced novel proteins over time and in different tissues in case of plants and animals which help in the formulation of risk hypothesis and subsequently risk assessment. The inheritance and stability of each introduced modification/trait i.e. functional in the modified organism must be determined. The first presumption for safety assessment of GMO is that the modified organism is as hazardous as the host. 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 transcript levels.

3.3.2 Human/Animal Health Considerations

The risk assessment initially considers a wide range of potential pathways. Those pathways that describe substantive risks should be considered in more detail and the level of risk evaluated. The result provides a qualitative measure of the risk, and allows a containment level to be assigned for the use of the organism.

The risk assessment strategy for genetically engineered (GE) organisms and derived food seeks to deploy appropriate methods and approaches to compare GE organisms and derived food with their appropriate comparators having a history of safe use. The underlying assumption of this comparative approach is that traditionally cultivated crops have a history of safe use for consumers. This approach focuses on determining whether any new or altered hazards are present, relative to existing conventional foods, with any identified hazards becoming the focus of further assessment. The Comparative Safety Assessment (CSA) of GE food is basically a two tiered approach.

The molecular characterization together with the comparative analysis of trait related to biochemical composition and phenotypic characteristics of GMO with the closely related conventional counterpart to identify differences that may have safety implications constitutes the first step.

The second step comprises of the toxicological, allergenic and nutritional evaluation of the identified differences. Impact on human/ animal 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.

3.3.3 Environmental Considerations

Risks associated with a GE organism is assessed in a structured, reasoned approach for determining the chance of harm from the environmental release of a GE organism, based on scientific evidence and taking into account any information received from subject experts and other stakeholders. The aim is to identify, characterize and evaluate risks to the health and safety of people or to the environment from the use of GE organism, when compared with risks posed by conventional varieties. The risk assessment begins by determining what could go wrong and how harm might occur if a particular GE organism was intentionally released into the environment. Risks are then characterized by considering how serious the harm could be (consequences) and how likely that harm could occur. The level of risk is then evaluated by integrating consequences and likelihood. In addition to the effect of inserted gene(s) or modified 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 impact 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.

In brief, IBSC shall undertake the risk and safety assessment of a GMO with reference to Molecular Biology, Human & Animal Health and Environmental Considerations as per details in Table 3 below:

TABLE 3: Broad categories of information/data required for GMO safety assessment Particulars

Broad categories data requirement	**Information Required**
Molecular Biology Details	
Characteristics of source (donor) organisms	▪ Origin/source and taxonomic classification ▪ Nature of pathogenicity and virulence, infectivity, allergenicity and toxicity, its host range and stability of these traits
Characteristics of host/recipient	▪ Origin/source and taxonomic classification ▪ Specific genotypic characters

organisms	▪ Information on reproductive biology, including, growth and development, reproductive cycle (asexual/sexual) details. For plants, information on floral biology, seed dormancy and dissemination of seeds. ▪ Nature of pathogenicity and virulence, infectivity, allergenicity and 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., modification(s) (e.g., codon optimization, amino acid substitution, truncation of transgenes) if any, made in native DNA sequence (from the source organism) of the genetic elements 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 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 and Animal Health Considerations	
Key Components	▪ Changes in the level of key nutrients, natural toxicants or anti-nutrients, secondary metabolites, physiologically active (bioactive) substances, etc.
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 allergens ▪ Heat stability and susceptibility of the expressed protein to pepsin digestion ▪ Studies such as immunoreactivity assessment, skin sensitization in animals, if required
Nutritional analysis	▪ Changes in the level of key nutrients, natural toxicants or anti nutrients, secondary metabolites, physiologically active (bioactive) substances, etc.
Environmental Considerations	
Considerations	▪ Changes in the growth, habit, life cycle, biomass and reproductive characteristics, response to biotic and abiotic stresses, changes in aggressiveness potential and weedy characters, non-target adverse effects etc. ▪ Disposal of biological material

3.4 RISK GROUPS AND CONTAINMENT FACILITIES

In general, biosafety begins with ensuring that the workplace (whether it is a laboratory, fermentation plant or open field) is safe for the working staff, the general public and the environment by proper containment/ confinement. Containment includes combination of facilities, practices and procedures for managing risk-inherent microorganisms, GE organisms or cells where they are being handled or maintained for reducing the exposure, preventing their escape within establishment and/ or in natural environment. The selection of containment facilities depend upon the risk category of microorganisms. The Risk Groups with details of microorganisms falling into each category and required containment facilities for each group are given in "The Regulations and Guidelines for Recombinant DNA Research & Biocontainment, 2017", Annexure 1. The list provided is indicative but not exhaustive and will be updated periodically. However, for working with organisms not listed in these guidelines, it is the responsibility of the investigator to determine appropriate risk groups and containment level in consultation with IBSC/RCGM.

3.4.1 Risk Groups of microorganisms

In case of microorganisms, the pathogenicity of the organism is extremely important for the risk assessment and its subsequent categorization. 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. Classification of microorganism into risk groups (see Table 4) is based on:

a. Pathogenicity of the organism towards humans/animals/plants.

b. Modes of transmission and host range of the organism.

c. Availability of effective preventive treatments or curative medicines.

d. Capability to cause epidemics.

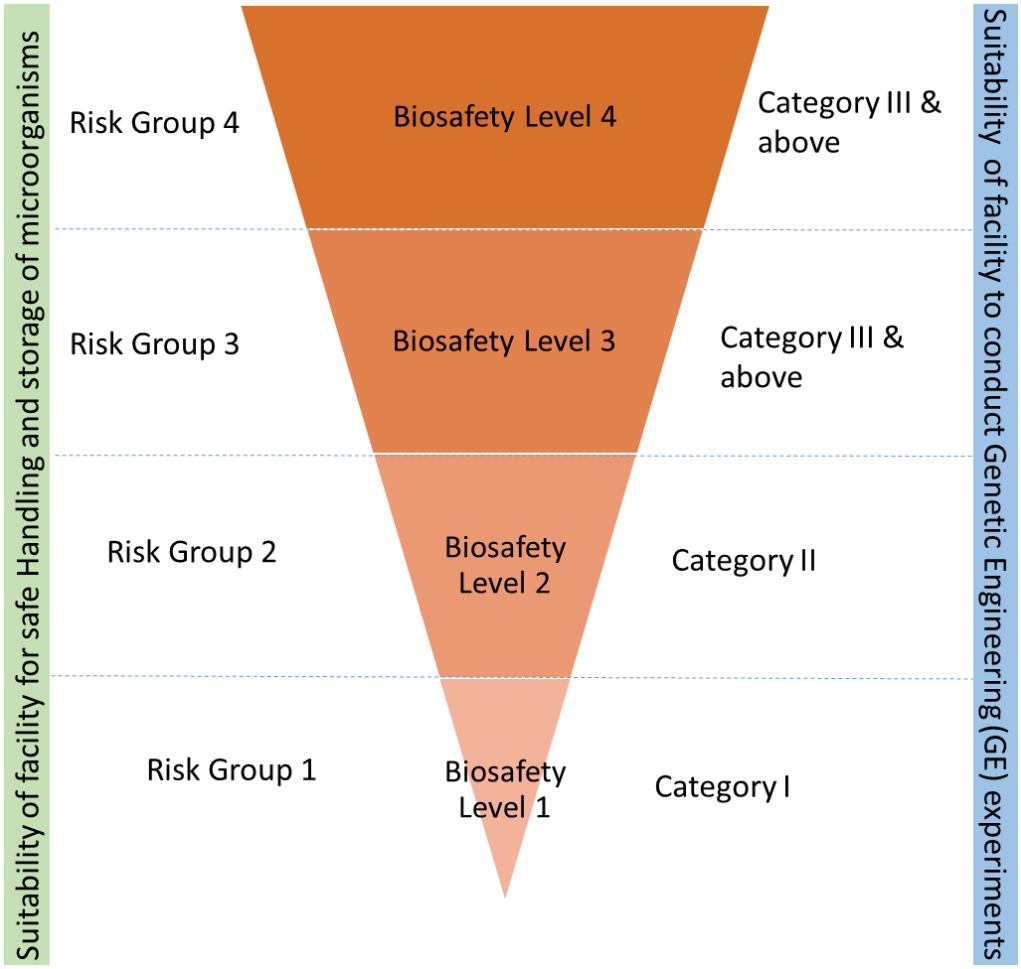
TABLE 4: Risk Group (RG) classification

Risk Group (RG)	Description
RG 1 (no or low individual and community risk)	Microorganism that are unlikely to cause human/ animal/plant disease
RG 2 (moderate individual risk, low community risk)	Microorganism that can cause disease in human /animal/ plant. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited
RG 3 (high individual risk, low community risk)	Microorganism that usually causes serious or lethal human/ animal/ plant disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.
RG 4 (high individual and community risk)	Microorganism that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

3.4.2 Categories of Genetically Engineered (GE) Experiments and Biosafety Level Facility Requirements

Considering fact that genetic engineering can alter/change the overall risk of an organism, a risk re-evaluation approach has been mentioned in these guidelines for the selection of appropriate containment facility. Operational details that are not specified in these guidelines shall be as per International best practices wherein the proposals shall be taken up in the IBSC meeting(s) for proper deliberations and approval before commencement of the work. Further, request for any change of an operational parameter(s) of a containment facility shall be evaluated by IBSC in the same manner before approval to ensure that the change does not affect the biosafety and biosecurity concerns that may arise while working in the facility.

Higher the risk group that the organism belongs to, higher is the risk involved: A guide for selection of appropriate containment facility for handling and storage microorganisms and conducting GE experiments is shown in Figure below:



Guide for selection of appropriate biosafety level laboratory for handling microorganisms and conducting GE experiment

3.5 OTHER GUIDELINES

IBSC shall also refer following guidelines:

- "Guidelines and Standard Operating Procedures (SOPs) for Confined Field Trials of Regulated, Genetically Engineered (GE) Plants 2008". This guideline not only assists in proper conduct of confined fields trials but also in transport and storage of regulated GE plant material, management, harvest or termination and post-harvest management, storage inspection, planting, spatial isolation, and monitoring of confined field trials of GE crop in the country.
- "Guidelines for the Environmental Risk Assessment of Genetically Engineered Plants, 2016" for generating data in a systematic and structured approach to their risk analysis.
- "Guidelines on Similar Biologics, 2016"
- "Guidelines for Generating Pre-Clinical and Clinical Data For r-DNA Based Vaccines, Diagnostics And Other Biologicals, 1999" for generating data for preclinical safety evaluation in a systematic and structured approach to cover safety, purity, potency and effectiveness of the product.
- "Guidelines for the Safety Assessment of Foods Derived from Genetically Engineered Plants, 2008" and/ "Protocols for Food and Feed Safety Assessment of GE crops, 2008".
- Approval procedures for import and export of GE plants and planting materials as described in the 'Procedure of Import and Export of GM Plants & Planting Material' published by GEAC, MoEF&CC.

Note: For further updates on the guidelines, IBSCs are advised to refer to IBKP and GEAC, MoEF&CC websites.

CHAPTER-IV: COMPLIANCE ADHERENCE

IBSC shall ensure storage and handling of HMOs, GE Organisms and related materials in accordance with the conditions specified in "Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017".Further, on-site emergency plan shall be prepared with adequate familiarity with the organisms being handled and detailed precautions while working with them. 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.

4.1 SUBMISSION OF DOCUMENTS FOR COMPLIANCE ON IBKP

a) The entire process of compliance submission is integrated into the IBKP where it is the responsibility of the utmost authority (Chairperson, IBSC) or his designate holding Organization's permanent login id and password to submit the requisite details timely to avoid cancellation of IBSC registration.

b) Each IBSC is required to upload following documents on Indian Biosafety Knowledge Portal (IBKP) under "Compliance Adherence" on IBSC DASHBOARD (http://ibkpdbt.gov.in). On clicking compliance adherence tab, screen with (1) Confidentiality Agreement (2) Minutes of the IBSC Meeting (3) Annual Compliance Report and (4) Medical Surveillance Report will appear where relevant documents shall be uploaded.

c) Annual Compliance report to be generated online in the format supplied in this section and to be uploaded with physical signatures. Each IBSC has to furnish an annual report (in the month of January not later than 15th February) along with Annual transaction record of IBSC to RCGM.

d) On successful submission of the compliance documents, IBSC shall be notified through the registered email id as well.

4.2 PERSONS RESPONSIBLE FOR COMPLIANCE ADHERANCE

a. Head of the Organisation

The head of the organisation shall be responsible:

- For compliance with Rules, 1989 and other related regulations regarding GE research.
- To bear ultimate responsibility for the safe conduct of activities involving HMOs/GMOs/LMOs/GE research.
- To ensure authorized access and proper storage of biological materials.
- To keep informed SBCC and DLC at all stages of rDNA work in the organization.

b. Principal Investigator (PI)

The responsibilities of PI are summarized below:

- Based on the RG of the GE organisms/LMOs and GE materials, the PI determines the proper containment level for the project and in accordance with the guidelines, develops the necessary experimental protocols.
- Depending upon the risk category experiments, the PI has to inform the IBSC for category-I experiments, seek permission of IBSC before starting the experiments for category-II or seek permission of the RCGM through its IBSC for category-III & above experiments.
- To make an initial determination of the required levels of physical and biological containment in the research activity to be under taken 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 or by RCGM/GEAC also as the case may be and has met all requirements of DBT guidelines.

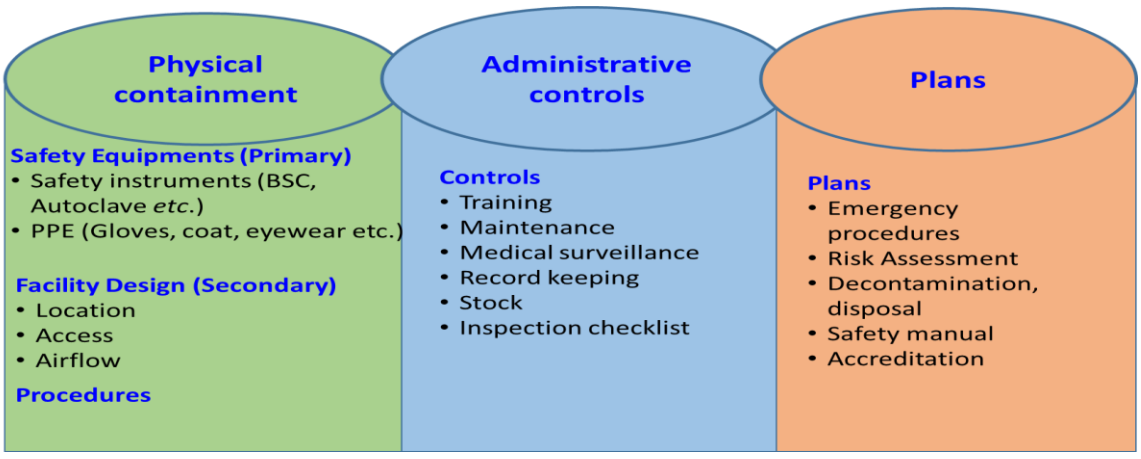
- To instruct laboratory staff about the practices and techniques required to ensure safety, and the procedures for dealing with accidents including the reasons and provisions for any precautionary medical practices advised or requested (e.g. vaccinations or serum collection).
- To supervise the performance of the laboratory staff to ensure that they 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.
- To properly treat the resulting Biowastes and also ascertain that organisms are either destroyed or rendered harmless before disposal into the environment.
- To undertake corrective measures promptly for any work errors/ accidental laboratory spillage and conditions that may result in the release of hazardous microorganisms, GE organisms and cells and products thereof.
- Submit annual progress report, Final report of the project to IBSC.
- Inform IBSC of premature termination of study/ experiment.
- 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).

4.3 COMPONENTS OF ON-SITE BIOSAFETY & EMERGENCY PLAN

IBSC to approve up-to-date on-site biosafety & emergency plan for each project according to the manuals/guidelines of the RCGM before any rDNA work is undertaken. IBSC shall make available copies of up-to-date on site biosafety & emergency plan to the District Level Committee (DLC)/State Biotechnology Co-ordination Committee (SBCC) and the Genetic Engineering Appraisal Committee (GEAC). The various components of on-site biosafety and emergency plan are:

a. Containment/Storage of Hazardous microorganisms/GE Organisms including storage facility and Related materials

- IBSC shall ensure storage of HMOs, GE Organisms and related materials in accordance with the conditions specified in "Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017".
- IBSC must evaluate the availability of proper containment facilities before the commencement of experiments. Containment facilities cover laboratory where genetic modifications are made and greenhouse or growth room and Net houses where they are grown for trials to assess trait efficacy and human and environment safety. Here safety of the workers and the environment is important. There is also a risk of accidental release where the waste from laboratories/fields is not carefully monitored and treated as per the prevailing laws, acts, rules and guidelines. Therefore, the containment requirements would take into account both impact on human health and environment. The containment could be physical, where there are real barriers to prevent escape or biological in nature where the organism is designed not to be able to survive in the environment other than the laboratory with specific conditions.



The facility design and related practices including laboratory monitoring, health and medical surveillance, decontamination and disposal strategies and emergency procedures for RG 1 to 4 for genetically engineered animal, plant, arthropods/ insect and aquatic organisms have been prescribed in 'Chapter 3: Operational Guides on Containment' in the 'Regulations and Guidelines for Recombinant DNA Research and Biocontainment, 2017'.

b. Health and Medical Surveillance

IBSC shall ensure that the health and medical surveillance of laboratory personnel is carried out by employing authority and/or project in-charge. The objectives of the health and medical surveillance of laboratory personnel are to prevent individuals from acquiring infection during the work, early detection of laboratory-acquired infection, assessing the efficacy of protective equipment and procedures, prophylactic vaccinations where needed and monitor booster regimens and assessment of sero conversion, in applicable cases.

c. Decontamination and Disposal

IBSC shall ensure selection of appropriate decontamination and disinfection strategies for laboratory and biomedical waste treatment and disposal waste should be as per the Biocontainment Guidelines and also in accordance the "Revised Guidelines for Common Bio-medical Waste Treatment and Disposal Facilities, 2016" issued by Central Pollution Control Board (CPCB) and local authorities.

IBSC may review the disposal methods. The potentially hazardous biological materials and HMOs/GMOs/LMOs/GE materials are to be considered as "regulated waste" and should be disposed of in a manner consistent with "Regulations and Guidelines for Recombinant DNA research and Biocontainment, 2017" and other stipulated guidelines issued from time to time by other agencies.

d. Emergency Procedures

IBSC should ensure that emergency contingency plans in consideration of every possible breach in biocontainment should be prepared for each individual laboratory as well as for the institution. These are best prepared by the individual laboratory supervisor in conjunction with his staff and the biosafety officer. This procedure offers the best prospect of success as it is the immediate staff that is most familiar with the hazards associated with a particular laboratory.

The PI must be conscientious of biosafety at all stages of handling of HMOs and rDNA work in the project including safeguard of GMO materials and should be held accountable for them. The PI, depending on the risk group organisms, HMOs/GMOs/LMOs and GE materials, should develop an on-site biosafety & emergency plan to protect the manpower & 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 HMOs/GMOs/LMOs and GE materials for routine cleaning, maintenance, and repairs, restricting unauthorized persons, addressing loss of keys, passwords and any other secured information, GE material etc.

4.4 REPORTING OF INCIDENTS AND ACCIDENTAL RELEASE

It is necessary that any incident within an organization such as non-compliance of the biosafety guidelines, any biosecurity issues or any significant research-related accidents and illnesses (e.g. exposure to any uncontained hazardous microorganisms, GE organisms and cells and products thereof, or contamination from equipment failure or a potential or over exposure in the BSL-3 or BSL-4) be reported by the PI to the IBSC Chairperson within 24 hours. Member secretary –IBSC/ Chairperson IBSC is responsible for reporting such incident to the DBT Nominee and RCGM within 48 hours from the incident. The DBT nominee shall assess the incident and send an independent report.

4.5 ADDRESSING NON-COMPLIANCE

Non-compliance can result in the IBSC taking one or more of the following actions:

i. Suspension of the use of HMOs/GMOs/LMOs/GE materials.

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

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

iv. Any other action deemed necessary to protect the public and environment, including suspension of all relevant research activity.

v. Reporting to the RCGM.

ANNEXURE-I: LIST OF FORMS/PERFORMA AVAILABLE ON IBKP

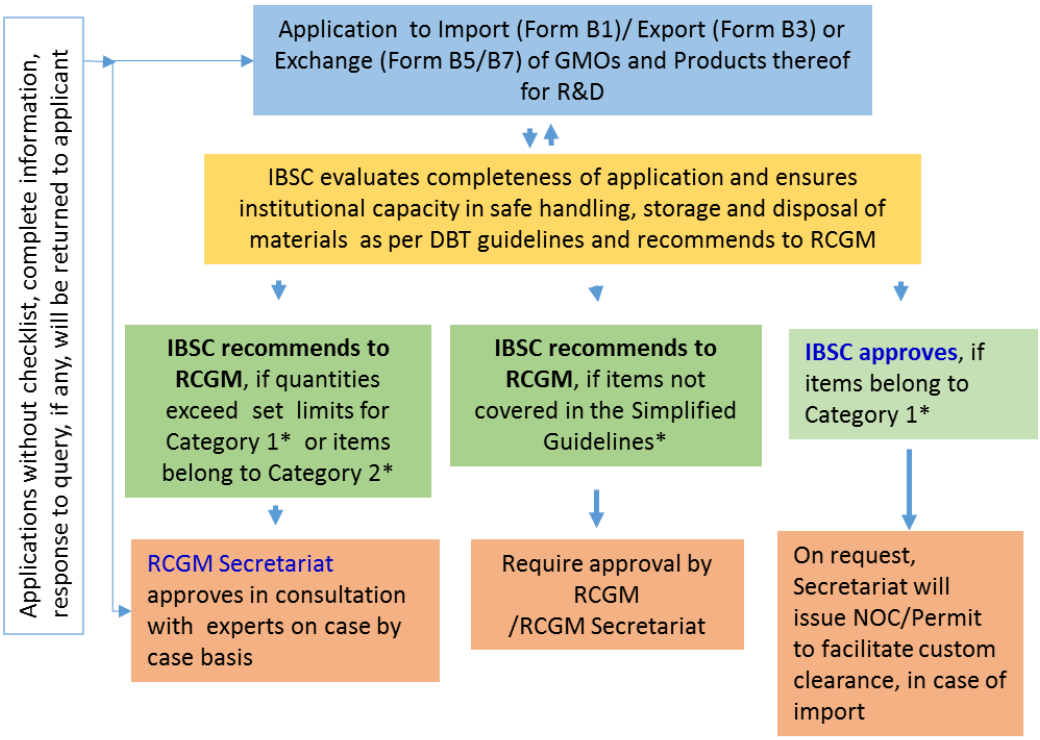
I. IBSC	
Performa of Medical Surveillance Report	
Performa of Confidentiality Agreement, CV and other formats	
Format of Minutes of IBSC	
Performa of Annual Compliance Report	
II. IMPORT, EXPORT, TRANSFER AND RECEIVE OF REGULATED MATERIAL FORM	
FORM B1	Application to RCGM for Import of HMOs, GMOs/LMOs and Product(S) Thereof For Research & Development Purpose
FORM B3	Application to RCGM for Export of HMOs/GMOs/LMOs & Product(S) Thereof For Research & Development Purpose
FORM B5	Application to RCGM for Receiving HMOs, GMOs/LMOs & Product(S) Thereof For Research & Development Purpose within India
FORM B7	Application to RCGM for Transfer of Hazardous Microorganisms (HMOs), Genetically Modified Organisms (GMOs)/Living Modified Organisms (LMOs) and Product(S) Thereof For Research and Development Purpose within India
III. ACTIVITIES INVOLVING RESEARCH, PRODUCTION, PRECLINICAL STUDIES OF GMOS IN HEALTHCARE/ACTIVITIES INVOLVING RESEARCH, PRODUCTION, PRECLINICAL AND OTHER STUDIES	
FORM C1	Information to RCGM to Carry Out Research and Development Involving Hazardous Microorganisms (HMOs), Genetically Modified Organisms (GMOs)/ Living Modified Organisms (LMOs) For Healthcare And Industrial Use
FORM C3a	Application to RCGM to Conduct Preclinical and/or Safety Studies of Similar Biologic Developed Using GMOs/ LMOs for Healthcare and Industrial Use
FORM C3b	Application to RCGM to Conduct Preclinical and/or Safety Studies of New DNA Product Developed Using GMOs/ LMOs

FORM C5a	Submission of Report of Preclinical or Other Safety Studies of Similar Biologic Developed Using GMOs/ LMOs
FORM C5b	Submission of Report of Preclinical or Other Safety Studies of New rDNA Product Developed Using Genetically Modified Organisms (GMOs)/ Living Modified
FORM F3	Submission of Report on Restricted Release Research Study/(ies)/ Trial(S) Of Genetically Engineered (GE) Arthropods for Agricultural, Healthcare and Environmental Use
IV. ACTIVITIES INVOLVING RESEARCH AND SAFETY STUDIES OF GE PLANTS	
FORM D1:	Information to RCGM to Carry Out Research and Development Involving Hazardous Microorganisms (HMOs), Genetically Modified Organisms (GMOs)/ Living Modified Organisms (LMOs) For Agricultural And Environmental Application
FORM D3 Event Selection:	Application to Undertake Confined Field Trial and To Undertake Safety Studies Of Genetically Engineered Crops/ Plants for Agricultural and Environmental Use
FORM D3 BRL-1:	Application to Undertake Confined Field Trial and To Undertake Safety Studies Of Genetically Engineered Crops/ Plants for Agricultural and Environmental Use
FORM D3 BRL-2:	Application to Undertake Confined Field Trial and To Undertake Safety Studies Of Genetically Engineered Crops/ Plants for Agricultural and Environmental Use
FORM D3 Other:	Application to Undertake Confined Field Trial and To Undertake Safety Studies Of Genetically Engineered Crops/ Plants for Agricultural and Environmental Use
FORM D7:	Submission of Report of Safety Studies of Genetically Engineered (GE) Crops/Plants for Agricultural and Environmental Use
FORM E3:	Submission of Report of Safety Studies of Hazardous Microorganisms (HMOs), Genetically Modified Organisms (GMOs)/ Living Modified Organisms (LMOs) Other Than GE Crops/ Plants for Agricultural and Environmental Use

FORM F3:	Submission of Report on Restricted Release Research Study(s)/ Trial(s) of Genetically Engineered (GE) Arthropods for Agricultural, Healthcare and Environmental Use

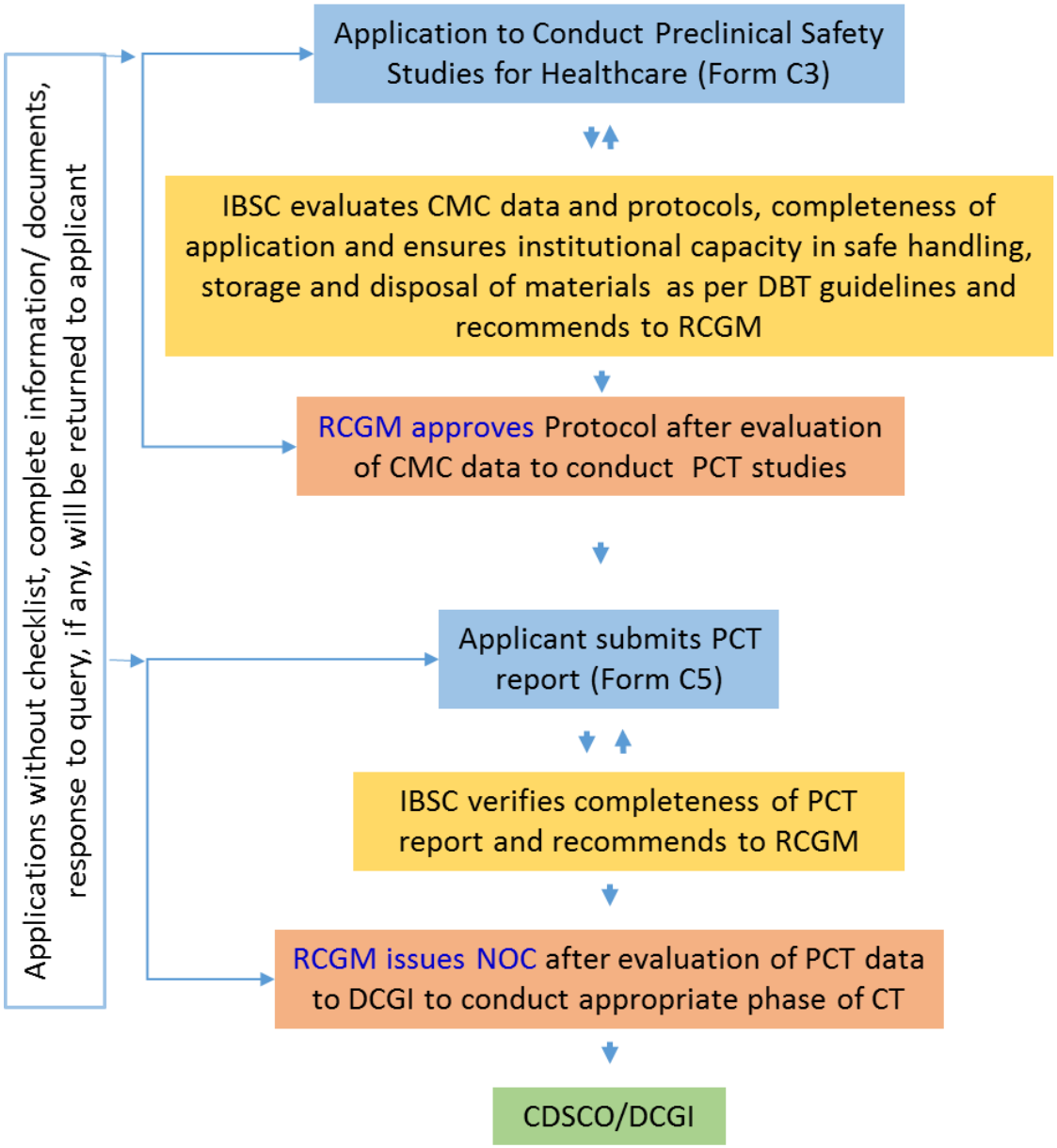
ANNEXURE-II: PATHWAY FOR REGULATORY APPROVALS

(a) Import/ Export/ Transfer/ Receive of regulated items

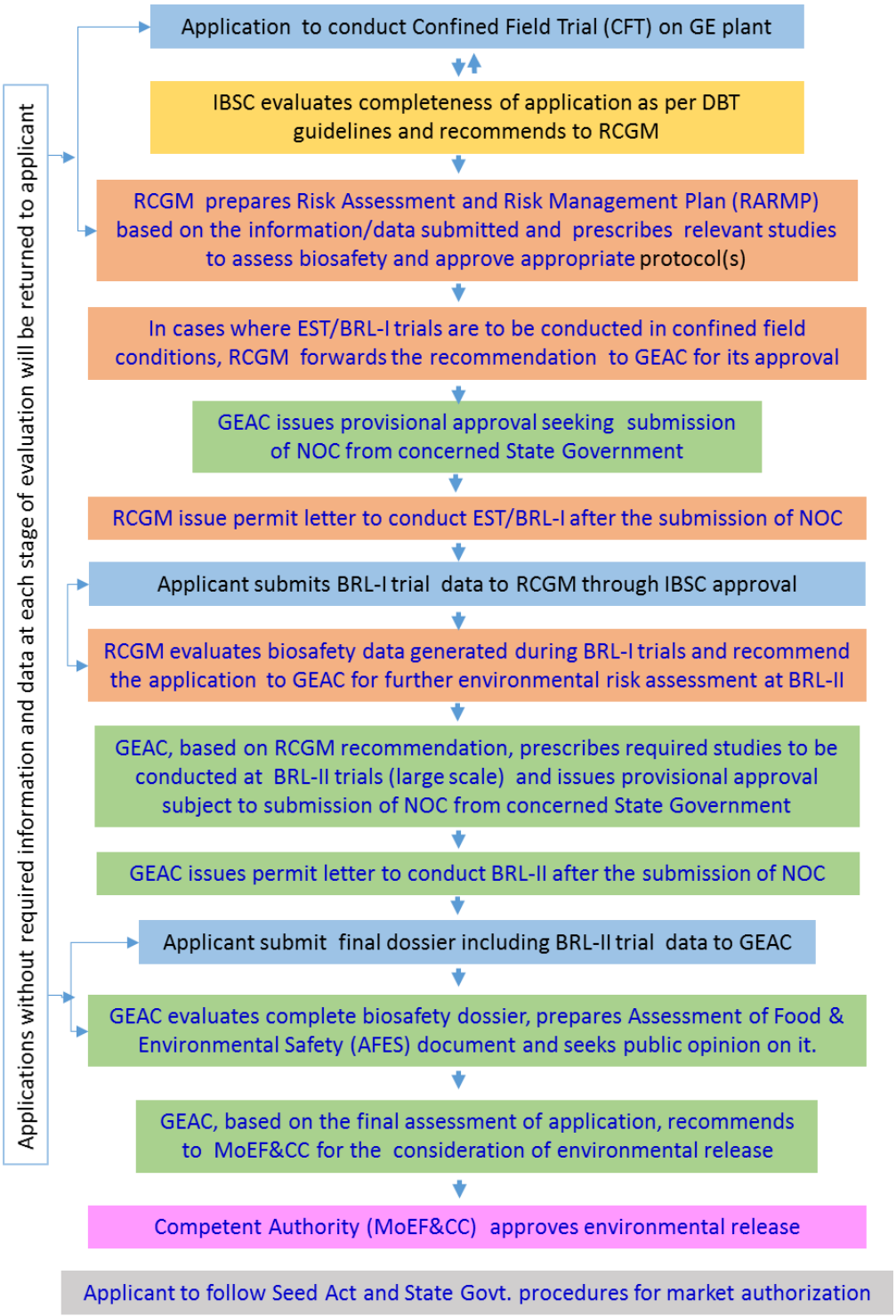


- *Refer Guidelines on Exchange (inter-state and inter- institutional supply/receipt within India), Import and Export of Genetically Engineered Organisms and product(s) thereof for Research purpose issued by DBT vide OM BT/BS/17/635/2015-PID dated 22.9.2015
- Based on RCGM approval, ICAR-NBPGR will issue permit letter and receive materials and pass on to applicant if import involves GMO plants/seeds
- Based on IBSC/RCGM permit, if export item belong to SCOMET list, applicant needs to apply to DGFT
- For export of biological material of Indian origin, National Biodiversity Authority of India permit is also required in addition to IBSC/RCGM permit

(b) Pre-Clinical & Safety studies of Healthcare products



(c) CFT on GE plants



ANNEXURE-III: REVISED SIMPLIFIED PROCEDURE/GUIDELINES ON IMPORT, EXPORT AND EXCHANGE OF REGULATED ITEMS, 2020

भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
बायोटेक्नोलॉजी विभाग
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

सूचना का अधिकार

ब्लाक-2,7 वां तल, सी० जी० ओ० कम्पलेक्स
लोदी रोड, नई दिल्ली-110003
Block-2, 7th Floor C.G.O. Complex
Lodi Road, New Delhi-110003

No. BT/BS/17/635/2015-PID **Dated 17.1.2020**

OFFICE MEMORANDUM

Sub: Revised Simplified Procedure/ Guidelines on Import, Export, and Exchange of GE organisms and product thereof for R&D purpose

In supersession of DBT's OM No BT/BS/17/635/2015-PID dated 22nd September 2015 notifying 'Simplified Procedure/ Guidelines on Import, Export, and Exchange of GE organisms and product thereof (Regulated items) for R&D purpose', RCGM in accordance with the provision in Rule 4, sub-clause 2 of The Manufacture, Use, Import, Export and Storage of Hazardous Micro-organisms/ Genetically Engineered Organisms or Cells Rules, 1989 under the Environment (Protection) Act, 1986 has approved following Simplified Procedures/Guidelines on Import, Export, and Exchange of Regulated items for R&D purpose to facilitate conduct of preclinical & safety studies and the product development at GMP facilities for biological drug development'.

a. IBSCs are authorized to consider and approve the applications for exchange, import or export of the regulated biological materials up to prescribed quantities as specified in Annexure 1.
b. For Research and Development leading to biopharma drug development, IBSC shall approve the import and export of permissible items upto the prescribed quantity(ies) following the approval procedure and conditions as specified in Table A of Annexure 1.
c. For Research and Development other than biopharma drug development, IBSC shall approve import, export, and exchange of permissible items in the prescribed quantity(ies) following the approval procedure and conditions as specified in Table B of Annexure 1.
d. Import, export, and exchange of Regulated items more than the specified quantity or not covered in the Annexure 1 will require approval from RCGM. The applicant shall submit an application, duly filled in every aspect, to RCGM through Indian Biosafety Knowledge Portal.
e. Preclinical and/or safety studies once approved by the sponsor IBSC and RCGM, CRO may conduct the study with intimation to the sponsor IBSC. CRO shall not require additional approval from CRO, IBSC and RCGM. However, reports generated by CRO shall be submitted to RCGM by sponsor IBSC.

2. All IBSCs and host institutions shall take note of these revised procedures / guidelines for compliance.

3. These revised Simplified Procedures/Guidelines and the instructions thereof may be reviewed by RCGM from time to time for necessary changes if any.

(Dr. Nitin K Jain)
Member Secretary, RCGM & Scientist F

To,

1. All IBSCs (Chairman & DBT Nominee) for information and compliance
2. Member Secretary, GEAC
3. Drug Controller General of India, CDSCO for information.

Copy to NIC- DBT for uploading on DBT Website & IBKP Portal.

Website: http://www.dbtindia.nic.in http://www.btisnet.gov.in
दूरभाष/Telephone : 24363012, 24362329 फैक्स/Fax : 011-24362884

Department of Biotechnology
Ministry of Science & Technology
File No. BT/BS/17/635/2015-PID (dated 17.01.2020)

Annexure 1

Revised Simplified Procedure/ Guidelines on Import, Export, and Exchange of Regulated items under Rules 1989 for R&D purpose [For exclusive use in containment for R&D purposes and not meant for release in the environment]

A. Import & Export of following items for Biopharma Drug Development R&D will require IBSC Approval.

Category	Quantity Proposed
1.1 Purified Nucleic acids Nucleic acids/ polynucleotides/ plasmid vector/ genetic constructs of natural/ synthetic/ recombinant origin and not present within or containing any host (living microorganisms/ cells) **Characteristics** a. Cannot produce infectious forms of any biological agent (for eg viruses) by itself when introduced into an animal or permissive cell or host or any other in vitro system with or without the introduction of rescue plasmids or other exogenous factors. b. Upon translation *in vivo* or *in vitro*, in a vector or recombinant host genome, do not produce a functional form of toxin that is lethal for vertebrates at LD_{50} of less than 1 microgram per kilogram body weight. c. Have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes on its own.	1 mg
1.2 Proteins A purified form of protein i.e. antigens, antibodies, proteinaceous vaccines, enzymes, toxins, hormones etc. of synthetic/ recombinant origin **Characteristics** a. Not toxic at LD_{50} of less than or equal to 1 microgram per kilogram body weight b. Not toxic at LD_{50} of less than or equal to 200 microgram per kilogram body weight	100 gm 20 gm 100 gm
1.3 Drug Products/ Drug Substances/ API/ Process intermediates **Characteristics** a. Do not contain or consist of living microorganisms b. Do not contain or consist of biological ingredients that render it harmful to humans	1 kg (concentration ranging between 0.05 gm/L to 180 gm/L)

1.4 Non-GE microorganism "Microorganisms" shall include all the bacteria, viruses, fungi, mycoplasma, cell lines, algae, protozoans and nematodes indicated in the schedule and those that have not been presently known to exist in the country or not have been discovered so far. **Characteristics** a. Belongs to Risk Group 1 and 2 b. Could be handled in BSL1 and BSL2 facility	**Cell lines** • 500 ml (10^{6-8} cells/ml) in liquid form • 200 gm lyophilized/ dry form **Microorganisms other than cell lines** • 200 ml (10^{6-8} cells/ml) in liquid form • 100 gm lyophilized/ dry form
1.5 GE Microorganisms A microorganism that is deliberately modified using rDNA technology and new gene technologies and contains plasmid vector/ expression constructs, etc of natural/ recombinant/ synthetic origin. **Characteristics (Refer Recombinant DNA Research and Biocontainment, Guidelines 2017)** a. Developed through Category I/ II genetic modification b. The host is routinely used in R&Ds and belongs to RG1 or RG2 and can be handled in BSL1/ BSL2 facility c. Host/vector system with or without any additional gene(s). The introduced gene(s) in the vector is completely characterized and should have features of nucleic acids mentioned in Section 1.1 d. Contain routine and standard mutations/ insertions that do not increase the overall risks e. DNA from Risk Group 2 and above agents is transferred into lower Risk Group microorganism f. Research Cell Bank (RCB)/ Working Cell Bank (WCB)/ Master Cell Bank (MCB) for use in drug development that can be handled in BSL1 and BSL2 facility	**GE Cell lines** • 500 ml (10^{6-8} cells/ml) in liquid form • 500 gm lyophilized/ dry form **GE Microorganisms other than cell lines** • 200 ml (10^{6-8} cells/ml) in liquid form • 200 gm lyophilized/ dry form
Exchange of regulated items within India (i.e. Transfer & Receive) for Biopharma Drug Development (R&D) shall not require approval from RCGM. The exchange of materials may take place with the approval from respective IBSCs of organizations involved in transfer/receive before commencing the activity. IBSCs shall include all such transactions in their annual reports and submit to RCGM through Indian Biosafety Knowledge Portal.	
Import and Export of Regulated items not specified or not covered in the above table will require approval from RCGM. All materials belonging to RG 3 and RG 4 require prior approval of IBSC followed by RCGM for transfer/exchange/ R & D. The applicant shall submit an application, duly filled in every aspect, to RCGM through Indian Biosafety Knowledge Portal.	

B. Exchange/Import/Export of following items for R&D other than Biopharma Drug Development will require IBSC Approval

Category	Containment	Quantity Permissible
1.1 Polynucleotides (of natural or synthetic or recombinant origin) a. Polynucleotides/ plasmids/ genetic constructs that cannot produce infectious forms of any biological agent (for eg viruses) by itself when introduced into an animal or permissive cell or host or any other in vitro system with or without the introduction of rescue plasmids or other exogenous factors. b. Those nucleic acids/polynucleotides that upon translation *in vivo* or *in vitro*, in a vector or recombinant host genome do not produce functional form of toxin that is lethal for vertebrates at LD_{50} of less than 1 microgram per kilogram body weight. c. Those nucleic acids/polynucleotides that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes on its own.	BSL1	100 µg
1.3 Proteins (including pure plant proteins) c. Those proteins that are not toxic at LD50 of less than or than equal to 1 microgram per kilogram body weight.	BSL 1	20 g
1.4 Non-living plant material	BSL 1	100 g
1.4 GE Microorganisms and Cell lines which can be handled at BSL 1 Containment a. Risk Group 1 microorganisms/cell lines b. DNA from Risk Group 2 and above agents (not involved in production of toxin, pathogenicity and allergenicity) is transferred into lower Risk Group microorganisms /cell lines which can be handled at BSL 1 containment facility	BSL1	20 vials (1-5 mL, 10^{6-8} cells /vial)
1.5 Model organisms: Plants (such as *Arabidopsis*), common laboratory models (such as *Ceanorhabditis, Drosophila, Danio* etc) and other model organisms (such as *Saccharomyces , Schizosaccharomyces, E. coli, Pichia and other model organisms) which are* routinely used in laboratories globally. The IBSC will certify that the plants/model organisms carry routine and standard experimental mutations/insertions and do not carry foreign gene-insertions from non-model organisms.	BL1-N/BL1-P/BL 1	For laboratory use only

Import/ Export/ Exchange of Regulated items more than the specified quantity or not covered in the above table will require approval from RCGM. The applicant shall submit an application, duly filled in every aspect, to RCGM through Indian Biosafety Knowledge Portal.

IBSC Approval Procedure and conditions

1. Approval by Sponsor's IBSC after examination of the information submitted by applicant to IBSC in prescribed proforma as per **Recombinant DNA Research and Biocontainment, Guidelines 2017.**
2. IBSC shall have to submit an annual report of transactions in prescribed proforma to RCGM through Indian Biosafety Knowledge Portal.
3. The applicant shall ensure that all relevant permissions are obtained before the commencement of the activity.
4. The export of dual use items falling under category 2 (Micro-organisms, toxins) of the SCOMET list, permission to export from DGFT shall be required. Information is available on www.dgft.gov.in.
5. On request, RCGM Secretariat may issue NOC/ permit based on IBSC approval, in case the applicant requests for the same for clearances from other Govt. agencies/Departments/ Custom.
6. Post import/export/exchange of Regulated items following IBSC approval, IBSC shall be responsible to monitor institutional safety resulting from the use of the items and conduct of R&D.

डॉ. नितिन कुमार जैन / Dr. NITIN K. JAIN
वैज्ञानिक 'एफ' / Scientist 'F'
बायोटेक्नोलॉजी विभाग / Deptt. of Biotechnology
विज्ञान और प्रौद्यो. मंत्रालय / M/o Science & Tech.
भारत सरकार, नई दिल्ली / Govt. of India, N. Delhi

ACKNOWLEDGEMENTS

- ✓ **Expert Committee** under the Chairmanship of Dr. P. Kondaiah, Professor, Indian Institute of Science (IISc), Bangalore; constituted by DBT for this purpose. Committee members include:
  - Dr. Debendra K. Sahoo, IMTECH, Chandigarh
  - Dr. Gururaj Katti, Indian Institute of Rice Research, Hyderabad
  - Member Secretary GEAC Ministry of Environment, Forests & Climate Change (MOEF&CC), New Delhi
  - Dr. Alka Sharma, Adviser, Scientist G, DBT, New Delhi
  - Dr. A.K. Rawat, Adviser, Scientist G, DBT, New Delhi
  - Dr. Vanga Siva Reddy, Chief Scientific Officer, Biosafety Support Unit, New Delhi
  - Dr. Nitin K Jain, Scientist F, DBT, New Delhi

- ✓ **Review Committee of Genetic Manipulation** (RCGM)

- ✓ Biosafety Support Unit, Regional Centre for Biotechnology, Faridabad
  - Dr. Sangeeta Agarwal, Chief Scientific Officer
  - Dr. Shipra Shahi, Scientist (Biochemistry)
  - Dr. Govind Kumar Rai, Scientist (Plant Biotechnology)
  - Dr. Manpreet Kaur, Scientist (Biosafety & Bio-containment)

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