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

सूचना का अधिकार

MINISTRY OF SCIENCE & TECHNOLOGY

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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.

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 <u>specified or not covered in the above table</u> 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.

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